



Clinical trial results:

Effects of GLP-1 Receptor Agonist Lixisenatide on Post-prandial Lipid Profile in Obese Type 2 Diabetic Patients

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-002263-15 |
| Trial protocol | IT |
| Global end of trial date | 04 August 2015 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 19 August 2016 |
| First version publication date | 19 August 2016 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | LIXISL07016 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-----------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02274740 |
| WHO universal trial number (UTN) | U1111-1153-3774 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Sanofi S.pA |
| Sponsor organisation address | Viale Bodio 37/b, Milan, Italy, 20158 |
| Public contact | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com |
| Scientific contact | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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 | 15 October 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 August 2015 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the ability of lixisenatide to modulate post-prandial hyperlipidemia as an add-on treatment to metformin in comparison to the control group (i.e . metformin therapy): in particular the effects on plasma changes in triglycerides in obese Type II diabetes subjects.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.

Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy:

Metformin was administered at a stable dose throughout the study unless there was a specific safety issue related to this treatment.

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 30 April 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|----------|
| Country: Number of subjects enrolled | Italy: 2 |
| Worldwide total number of subjects | 2 |
| EEA total number of subjects | 2 |

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) | 2 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at a single center in Italy between April 30, 2015 and August 04, 2015.

Pre-assignment

Screening details:

A total of 3 subjects were screened, of which 1 subject was screen failure due to HbA1c and triglycerides out of required range. 2 subjects were randomized.

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 | Lixisenatide + Metformin |

Arm description:

Lixisenatide 10 mcg once daily (QD) subcutaneously for 2 weeks, then at a maintenance dose of 20 mcg up to 10 weeks on top of metformin.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Lixisenatide |
| Investigational medicinal product code | AVE0010 |
| Other name | Lyxumia® |
| Pharmaceutical forms | Solution for injection in pre-filled pen |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Lixisenatide was self-administered QD by subcutaneous injection over 60 minutes before breakfast.

| | |
|------------------|-----------|
| Arm title | Metformin |
|------------------|-----------|

Arm description:

Metformin at a stable dose of ≥ 1.5 g/day as background therapy up to 10 weeks.

| | |
|---|---------------|
| Arm type | Control Group |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 1 | Lixisenatide + Metformin | Metformin |
|--------------------------------|--------------------------|-----------|
| Started | 1 | 1 |
| Completed | 1 | 0 |
| Not completed | 0 | 1 |
| Study interruption | - | 1 |

Baseline characteristics

Reporting groups

| | |
|--|--------------------------|
| Reporting group title | Lixisenatide + Metformin |
| Reporting group description: Lixisenatide 10 mcg once daily (QD) subcutaneously for 2 weeks, then at a maintenance dose of 20 mcg up to 10 weeks on top of metformin. | |
| Reporting group title | Metformin |
| Reporting group description: Metformin at a stable dose of ≥ 1.5 g/day as background therapy up to 10 weeks. | |

| Reporting group values | Lixisenatide + Metformin | Metformin | Total |
|---------------------------------------|--------------------------|-----------|-------|
| Number of subjects | 1 | 1 | 2 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 1 | 1 | 2 |
| Gender categorical Units: Subjects | | | |
| Female | 1 | 1 | 2 |
| Male | 0 | 0 | 0 |

End points

End points reporting groups

| | |
|--|--------------------------|
| Reporting group title | Lixisenatide + Metformin |
| Reporting group description: Lixisenatide 10 mcg once daily (QD) subcutaneously for 2 weeks, then at a maintenance dose of 20 mcg up to 10 weeks on top of metformin. | |
| Reporting group title | Metformin |
| Reporting group description: Metformin at a stable dose of ≥ 1.5 g/day as background therapy up to 10 weeks. | |

Primary: Change From Baseline in Triglycerides Area Under the Curve (AUC0-480 min) to Week 10

| | |
|---|---|
| End point title | Change From Baseline in Triglycerides Area Under the Curve (AUC0-480 min) to Week 10 ^[1] |
| End point description: AUC (0-480) was defined as the area under plasma concentration versus time curve from time 0 to 480 min after the meal. | |
| End point type | Primary |
| End point timeframe: 0 (pre-prandial) to 480 minutes after meal test at Baseline and Week 10 | |

Notes:

[1] - 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: Due to premature study interruption, none of the planned efficacy analysis was performed.

| End point values | Lixisenatide + Metformin | Metformin | | |
|--------------------------------------|--------------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[2] | 0 ^[3] | | |
| Units: Not applicable | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[2] - Due to premature study interruption, none of the planned efficacy analysis was performed.

[3] - Due to premature study interruption, none of the planned efficacy analysis was performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Triglycerides AUC0-480 min to Day 2

| | |
|---|---|
| End point title | Change From Baseline in Triglycerides AUC0-480 min to Day 2 |
| End point description: AUC (0-480) was defined as the area under plasma concentration versus time curve from time 0 to 480 min after the meal. | |
| End point type | Secondary |
| End point timeframe: 0 (pre-prandial) to 480 minutes after meal test at Baseline and Day 2 | |

| End point values | Lixisenatide + Metformin | Metformin | | |
|--------------------------------------|--------------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[4] | 0 ^[5] | | |
| Units: Not applicable | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[4] - Due to premature study interruption, none of the planned efficacy analysis was performed.

[5] - Due to premature study interruption, none of the planned efficacy analysis was performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Plasma Cholesterol, Apo B48, Free Fatty Acid, Lipoprotein to Day 2 and Week 10

| | |
|-----------------|--|
| End point title | Change From Baseline in Plasma Cholesterol, Apo B48, Free Fatty Acid, Lipoprotein to Day 2 and Week 10 |
|-----------------|--|

End point description:

Change was to be calculated by subtracting baseline values from Day 2 and Week 10 values.

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

End point timeframe:

0 (pre-prandial) to 480 minutes after meal test at Baseline, Day 2 and Week 10

| End point values | Lixisenatide + Metformin | Metformin | | |
|--------------------------------------|--------------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[6] | 0 ^[7] | | |
| Units: Not applicable | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[6] - Due to premature study interruption, none of the planned efficacy analysis was performed.

[7] - Due to premature study interruption, none of the planned efficacy analysis was performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Low Density Lipoprotein (LDL) Oxidation to Day 2 and Week 10

| | |
|-----------------|--|
| End point title | Change From Baseline in Low Density Lipoprotein (LDL) Oxidation to Day 2 and Week 10 |
|-----------------|--|

End point description:

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

End point timeframe:

0 (pre-prandial) to 480 minutes after meal test at Baseline, Day 2 and Week 10

| End point values | Lixisenatide + Metformin | Metformin | | |
|--------------------------------------|--------------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[8] | 0 ^[9] | | |
| Units: Not applicable | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[8] - Due to premature study interruption, none of the planned efficacy analysis was performed.

[9] - Due to premature study interruption, none of the planned efficacy analysis was performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Post Prandial Plasma Glucose AUC0-480 min, Post Prandial Insulin AUC0-480 min; Post Prandial C-peptide AUC0-480 min to Day 2 and Week 10

| | |
|-----------------|--|
| End point title | Change From Baseline in Post Prandial Plasma Glucose AUC0-480 min, Post Prandial Insulin AUC0-480 min; Post Prandial C-peptide AUC0-480 min to Day 2 and Week 10 |
|-----------------|--|

End point description:

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

End point timeframe:

0 (pre-prandial) to 480 minutes after meal test at Baseline, Day 2 and Week 10

| End point values | Lixisenatide + Metformin | Metformin | | |
|--------------------------------------|--------------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[10] | 0 ^[11] | | |
| Units: Not applicable | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[10] - Due to premature study interruption, none of the planned efficacy analysis was performed.

[11] - Due to premature study interruption, none of the planned efficacy analysis was performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Cytokines and Stress Oxidative Markers to Day 2 and Week 10

| | |
|-----------------|---|
| End point title | Change From Baseline in Cytokines and Stress Oxidative Markers to Day 2 and Week 10 |
|-----------------|---|

End point description:

Cytokines and stress oxidative markers are indication of low grade inflammation.

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

End point timeframe:

0 (pre-prandial) to 480 minutes after meal test at Baseline, Day 2 and Week 10

| End point values | Lixisenatide + Metformin | Metformin | | |
|--------------------------------------|--------------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[12] | 0 ^[13] | | |
| Units: Not applicable | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[12] - Due to premature study interruption, none of the planned efficacy analysis was performed.

[13] - Due to premature study interruption, none of the planned efficacy analysis was performed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Coronary Flow Reserve (CFR) to Day 2 and Week 10

| | |
|-----------------|--|
| End point title | Change From Baseline in Coronary Flow Reserve (CFR) to Day 2 and Week 10 |
|-----------------|--|

End point description:

CFR was a ratio of coronary blood flow velocity before and after adenosine.

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

End point timeframe:

0 (pre-prandial) to 480 minutes after meal test at Baseline, Day 2 and Week 10

| End point values | Lixisenatide + Metformin | Metformin | | |
|--------------------------------------|--------------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[14] | 0 ^[15] | | |
| Units: Not applicable | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[14] - Due to premature study interruption, none of the planned efficacy analysis was performed.

[15] - Due to premature study interruption, none of the planned efficacy analysis was performed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected from signature of the informed consent form up to the final visit (Day 73) regardless of seriousness or relationship to investigational product

Adverse event reporting additional description:

No adverse event was reported during the trial.

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

Dictionary used

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

| | |
|--------------------|---|
| Dictionary version | 0 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | Lixisenatide + Metformin |
|-----------------------|--------------------------|

Reporting group description:

Lixisenatide 10 mcg once daily (QD) subcutaneously for 2 weeks, then at a maintenance dose of 20 mcg up to 10 weeks on top of metformin.

| | |
|-----------------------|-----------|
| Reporting group title | Metformin |
|-----------------------|-----------|

Reporting group description:

Metformin at a stable dose of ≥ 1.5 g/day as background therapy up to 10 weeks.

| Serious adverse events | Lixisenatide + Metformin | Metformin | |
|---|--------------------------|---------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 1 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Lixisenatide + Metformin | Metformin | |
|---|--------------------------|---------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 1 (0.00%) | |

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No adverse event was reported during the trial.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 16 September 2014 | - Changes in sections relative to the primary objective and primary endpoint sections were made for major clarity and internal consistency. - Changes in sections relative to the statistical analysis and pertinent to comparisons between groups were made for major clarity and internal consistency. - Changes in sections relative to the management of concomitant diabetes therapy were made to better clarify the procedures for the management of rescue therapy. - Exclusion criterion referring to renal disease was modified and the reference parameter and value was reworded according to estimated creatinine clearance ≤ 50 ml/min. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported