



## 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
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##### 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
<b>Arm title</b>	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.

<b>Arm title</b>	Metformin
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Arm description:

Metformin at a stable dose of  $\geq 1.5$  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 $\geq 1.5$ 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 $\geq 1.5$ 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 <sup>[1]</sup>
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 <sup>[2]</sup>	0 <sup>[3]</sup>		
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 <sup>[4]</sup>	0 <sup>[5]</sup>		
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
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End point description:

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

End point type	Secondary
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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 <sup>[6]</sup>	0 <sup>[7]</sup>		
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
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End point description:

End point type	Secondary
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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 <sup>[8]</sup>	0 <sup>[9]</sup>		
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
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End point description:

End point type	Secondary
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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 <sup>[10]</sup>	0 <sup>[11]</sup>		
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
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End point description:

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

End point type	Secondary
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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 <sup>[12]</sup>	0 <sup>[13]</sup>		
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
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End point description:

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

End point type	Secondary
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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 <sup>[14]</sup>	0 <sup>[15]</sup>		
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<sup>[1]</sup>

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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	0
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### Reporting groups

Reporting group title	Lixisenatide + Metformin
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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
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Reporting group description:

Metformin at a stable dose of  $\geq 1.5$  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 $\leq 50$ ml/min.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported