Clinical trial results:
A bicentric open-label, randomized, two-parallel-group study investigating the impact of combined Lantus®(insulin glargine) and Lyxumia ®(lixisenatide) on insulin secretion and gastric emptying in subjects with Type 2 Diabetes Mellitus not adequately controlled on diet and oral antidiabetic medication

Summary

EudraCT number	2013-003171-35
Trial protocol	DE
Global end of trial date	28 October 2015

Results information

Result version number	v1 (current)
This version publication date	07 February 2020
First version publication date	07 February 2020

Trial information

Trial identification

Sponsor protocol code	LanLyx

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01910194
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Profil Institut für Stoffwechselforschung GmbH
Sponsor organisation address	Hellersbergstr. 9, Neuss, Germany, 41460
Public contact	Regulatory Affairs, Profil Institut für Stoffwechselforschung GmbH, +49 21314018145, regulatory@profil.com
Scientific contact	Regulatory Affairs, Profil Institut für Stoffwechselforschung GmbH, +49 21314018145, regulatory@profil.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	08 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 October 2014
Global end of trial reached?	Yes
Global end of trial date	28 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To address in type 2 diabetic patients compared to baseline the effect of repeated doses of Lyxumia® and Lantus® after an eight weeks two-step treatment regimen (four weeks administration of either Lyxumia® or Lantus®, both followed by their combined administration for another four weeks) on intravenous glucose tolerance test (IVGTT) related first phase insulin secretion

Protection of trial subjects:

Since the launch of GLP-1 receptor agonists, very rare cases of pancreatitis have been reported in subjects receiving this treatment. Therefore, amylase and lipase will be monitored in this study. As this monitoring may be difficult in subjects who already have high values of amylase or lipase, subjects with values above 3 times the upper limit of normal range at screening, will not be entered in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 December 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 28
Worldwide total number of subjects	28
EEA total number of subjects	28

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)	16
From 65 to 84 years	12

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at two clinical sites in Germany.

Pre-assignment

Screening details:

In total, 43 subjects were screened and 28 subjects were included in the trial and randomised to one of the two possible treatment arms.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Treatment period 1 - Iglar

Arm description:

Insulin glargine administration

Arm type	Experimental
Investigational medicinal product name	Insulin glargine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

60 days of treatment, IMP will be titrated to achieve glycemic targets without hypoglycemia.

Arm title	Treatment period 2 / Lixi-Iglar

Arm description:

Lixisenatide plus Insulin glargine administration

Arm type	Experimental
Investigational medicinal product name	Lixisenatide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in cartridge
Routes of administration	Subcutaneous use

Dosage and administration details:

treatment duration 60 days; up to 20 µg microgram(s)/day

Investigational medicinal product name	Insulin glargine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

60 days of treatment, IMP will be titrated to achieve glycemic targets without hypoglycemia.

Arm title	Treatment period 1 - Lixi

Arm description:

Lixisenatide administration

Arm type	Experimental
Investigational medicinal product name	Lixisenatide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in cartridge
Routes of administration	Subcutaneous use

Dosage and administration details:
treatment duration 60 days; up to 20 µg microgram(s)/day

Arm title	Treatment period 2 / Iglar-Lixi

Arm description:
Insulin glargine plus Lixisenatide administration

Arm type	Experimental
Investigational medicinal product name	Lixisenatide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in cartridge
Routes of administration	Subcutaneous use

Dosage and administration details:
treatment duration 60 days; up to 20 µg microgram(s)/day

Investigational medicinal product name	Insulin glargine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:
60 days of treatment, IMP will be titrated to achieve glycemic targets without hypoglycemia.

Number of subjects in period 1	Treatment period 1 - Iglar	Treatment period 2 / Lixi-Iglar	Treatment period 1 - Lixi
Started	14	13	14
Completed	13	13	13
Not completed	1	0	1
Physician decision	-	-	1
Adverse event, non-fatal	1	-	-

Number of subjects in period 1	Treatment period 2 / Iglar-Lixi
Started	13
Completed	13
Not completed	0
Physician decision	-
Adverse event, non-fatal	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	28	28	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	16	16	
From 65-84 years	12	12	
85 years and over	0	0	
Age continuous Units: years			
median	60.2		
full range (min-max)	30 to 69	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	25	25	

End points

End points reporting groups	
Reporting group title	Treatment period 1 - Iglar
Reporting group description: Insulin glargine administration	
Reporting group title	Treatment period 2 / Lixi-Iglar
Reporting group description: Lixisenatide plus Insulin glargine administration	
Reporting group title	Treatment period 1 - Lixi
Reporting group description: Lixisenatide administration	
Reporting group title	Treatment period 2 / Iglar-Lixi
Reporting group description: Insulin glargine plus Lixisenatide administration	

Primary: AUCISEC(0-10min) - First phase insulin secretion	
End point title	AUCISEC(0-10min) - First phase insulin secretion
End point description:	
End point type	Primary
End point timeframe: 0-10 min	

End point values	Treatment period 1 - Iglar	Treatment period 2 / Lixi-Iglar	Treatment period 1 - Lixi	Treatment period 2 / Iglar-Lixi
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	13	13	11
Units: pmol h/L				
arithmetic mean (standard deviation)	0.198 (± 0.1684)	0.741 (± 0.3525)	0.386 (± 0.3334)	0.726 (± 0.5023)

Statistical analyses

Statistical analysis title	Efficacy Analysis Set - Iglar
Comparison groups	Treatment period 1 - Iglar v Treatment period 2 / Iglar-Lixi
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0062
Method	ANCOVA

Statistical analysis title	Efficacy Analysis Set - Lixi
Comparison groups	Treatment period 2 / Lixi-Iglar v Treatment period 1 - Lixi
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0394
Method	ANCOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall trial	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 28 (71.43%)		
Investigations			
Troponin I increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Lipase increased			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Amylase increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			

subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 6 / 28 (21.43%) 6		
General disorders and administration site conditions Application site erythema subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1		
Eye disorders Visual field defect subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 1		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	 1 / 28 (3.57%) 2 1 / 28 (3.57%) 1 3 / 28 (10.71%) 6 1 / 28 (3.57%) 1 2 / 28 (7.14%) 3 2 / 28 (7.14%) 2 1 / 28 (3.57%) 1		

Abdominal distension subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Respiratory, thoracic and mediastinal disorders Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2		

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