Clinical trial results:
Effects of once-daily administered GLP-1 Receptoragonist Lixisenatide in combination with basal Insulin on glycemic control in patients with type-2 diabetes mellitus not achieving therapeutic targets with premixed insulin strategy

Summary

EudraCT number	2013-005334-37
Trial protocol	AT
Global end of trial date	26 January 2016

Results information

Result version number	v1 (current)
This version publication date	14 October 2017
First version publication date	14 October 2017
Summary attachment (see zip file)	lixibit summary (LIXIBITSummary.pdf) Switch to Combined GLP1 Receptor Agonist Lixisenatide with Basal Insulin Glargine in Poorly Controlled T2DM Patients with Premixed Insulin Therapy: A Clinical Observation and Pilot Study in Nine Patie (13300_2017_Article_249.pdf)

Trial information

Trial identification

Sponsor protocol code	LixiBit

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02168491
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical University Vienna
Sponsor organisation address	Spitalgasse 23, Vienna, Austria, 1090
Public contact	Medical University of Vienna, Medical University of Vienna, michael.krebs@meduniwien.ac.at
Scientific contact	Medical University of Vienna, Medical University of Vienna, michael.krebs@meduniwien.ac.at

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	23 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Introduction of basal insulin therapy in combination with the GLP-1 receptor agonist Lixisenatide in patients with type-2 diabetes previously treated with premixed insulin not achieving therapeutic target will be associated with positive effects on glycemic control:
- Changes in HbA1c from baseline to end

Protection of trial subjects:

serious adverse events and adverse events reported.
laboratory measurements and vital signs every visit

Background therapy:

premixed insulin

Evidence for comparator:

Premixed insulin-based therapy is a standard insulin treatment strategy in Austria. The widespread use of premixed insulin is explained by high acceptance by health care professionals and patients due to one single product and flexible number of injections (1-3 daily) which covers the demand in controlling fasting and postprandial glucose excursions of most patients with diabetes. However, the use of pre-mixed insulin frequently leads to a high insulin demand and consequently weight gain and an increased risk of hypoglycemia. Hence, achieve good metabolic control in these patients remains a major challenge.

For those patients, the approach to treatment intensification without facing the typical risks of insulin treatment (hypoglycemia and weight increase) is of major importance. One, so far not exploited option may be the BIT-strategy: Basal insulin in combination with incretin-based therapy.

Pathophysiologically basal insulin inhibits glucose production in the liver, decreases hepatic insulin resistance and improves the function of beta cells in the postprandial state by discharge of fasting insulin secretion. During further diabetes progression steadily increasing HbA1c levels - despite good fasting blood glucose control - indicate the need for additional intervention of meal-related glucose excursions. In this stage of type-2 diabetes basal insulin can be combined with prandial (short-acting) insulin or prandial GLP-1 receptor agonists. However, regarding important safety parameters: risks of hypoglycemia and weight gain in the long-term treatment GLP-1 receptor agonists are beneficial.

Lixisenatide is a novel GLP-1 receptor agonist with a pronounced postprandial (PPG) effect which fits with basal insulin mode of action primarily focused on fasting blood glucose reduction.

Therefore 10 patients (both gender) under treatment with premixed insulin (2-3 times daily) and HbA1c>7% will be switched to basal insulin glargine (Lantus, once daily) and GLP-1 re

Actual start date of recruitment	01 July 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	Austria: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

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)	4
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

11 patients were screened
Study Start Date: November 2014
Study Completion Date: August 2015
Primary Completion Date: July 2015 (Final data collection date for primary outcome measure)
Austria, Vienna

Pre-assignment

Screening details:

2 patients declined to participate because of time restraints, thus study medication was administered in 9 patients

Period 1

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

Blinding implementation details:

Intervention Model: Single Group Assignment
Masking: None (Open Label)
Primary Purpose: Treatment

Arms

Arm title	Lixisenatide and Insulin Glargine

Arm description:

10 type 2 diabetic patients will be included to perform in this study and will be switched from premixed insulin to insulin glargine and lixisenatide

Arm type	Experimental
Investigational medicinal product name	Lixisenatide
Investigational medicinal product code	
Other name	Lyxumia
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

once daily in the morning before breakfast; days 1-14 10 µg thereafter 20 µg

Investigational medicinal product name	Insulin Glargine
Investigational medicinal product code	
Other name	Lantus
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The (mean) daily dose of premixed insulin will be calculated based on the records of the run in period. The initial dose of insulin glargine will be adjusted at about 60% of the daily insulin dose of premixed insulin.

Number of subjects in period 1	Lixisenatide and Insulin Glargine
Started	9
Completed	8
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	9	9	
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	65.6		
standard deviation	± 6	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	6	6	

End points

End points reporting groups

Reporting group title	Lixisenatide and Insulin Glargine

Reporting group description:

10 type 2 diabetic patients will be included to perform in this study and will be switched from premixed insulin to insulin glargine and lixisenatide

Primary: Change in HbA1c From Baseline to End

End point title	Change in HbA1c From Baseline to End[1]

End point description:

End point type	Primary

End point timeframe:

12 Weeks from baseline to end

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: baseline to end analysis was not possible to enter, analysis performed with a paired t test. attachment with additional information includes those about statistical analysis

End point values	Lixisenatide and Insulin Glargine			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: %				
arithmetic mean (standard deviation)	-0.54 (± 0.52)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12 weeks, baseline to end

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

Reporting groups

Reporting group title	endocrine disorders

Reporting group description:

mild asymptomatic hypoglycaemia
participants affected / at risk 3/9 (33.33%)
events 8
symptomatic hypoglycaemia
participants affected / at risk 1/9 (11.11%)
events 1
hypercholesterolaemia
participants affected / at risk 2/9 (22.22%)
events 2

Reporting group title	eye disorders

Reporting group description:

elective ambulatory cataract surgery

Reporting group title	gastrointestinal disorders

Reporting group description:

mild gastrointestinal complaints

Reporting group title	general disorders

Reporting group description:

cough

Reporting group title	infections and infestations

Reporting group description:

urinary tract infection

Reporting group title	musculoskeletal and connective tissue disorders

Reporting group description:

shoulder pain

Reporting group title	renal and urinary disorders

Reporting group description:

haematuria

Reporting group title	surgical and medical procedures

Reporting group description: -

Serious adverse events	endocrine disorders	eye disorders	gastrointestinal disorders
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Surgical and medical procedures			
Elective surgery	Additional description: ENT surgery		
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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	general disorders	infections and infestations	musculoskeletal and connective tissue disorders
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Elective surgery	Additional description: ENT surgery		
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 1 (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	renal and urinary disorders	surgical and medical procedures	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Elective surgery	Additional description: ENT surgery		
subjects affected / exposed	0 / 1 (0.00%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	endocrine disorders	eye disorders	gastrointestinal disorders
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	1 / 1 (100.00%)	0 / 2 (0.00%)
Endocrine disorders			
mild hypoglycaemic events			

subjects affected / exposed	3 / 6 (50.00%)	1 / 1 (100.00%)	0 / 2 (0.00%)
occurrences (all)	3	1	0

Non-serious adverse events	general disorders	infections and infestations	musculoskeletal and connective tissue disorders
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
Endocrine disorders			
mild hypoglycaemic events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	renal and urinary disorders	surgical and medical procedures	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	
Endocrine disorders			
mild hypoglycaemic events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28357772