Clinical trial results:
A phase 4, monocenter, randomized, open label, comparator-controlled, parallel-group, mechanistic intervention trial to assess the effect of 8-week treatment with the glucagon-like peptide-1 receptor agonist lixisenatide versus insulin glulisine on renal physiology and biomarkers in insulin glargine-treated patients with type 2 diabetes mellitus

Summary

EudraCT number	2014-002178-35
Trial protocol	NL
Global end of trial date	14 August 2019

Results information

Result version number	v1 (current)
This version publication date	26 November 2021
First version publication date	26 November 2021

Trial information

Trial identification

Sponsor protocol code	DC2014ELIX001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1151-0579

Notes:

Sponsors

Sponsor organisation name	VU University Medical Center
Sponsor organisation address	De Boelelaan 1117, Amsterdam, Netherlands,
Public contact	Lennart Tonneijck, VU University Medical Center, 0031 0204440651, l.tonneijck@vumc.nl
Scientific contact	Lennart Tonneijck, VU University Medical Center, 0031 0204440651, l.tonneijck@vumc.nl

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	21 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 August 2019
Global end of trial reached?	Yes
Global end of trial date	14 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective: To assess the long-term effects (i.e. after 8-week drug exposure) of the GLP-1RA lixisenatide versus insulin glulisine on renal hemodynamics (glomerular filtration rate/effective renal plasma flow) in patients with type 2 diabetes

Protection of trial subjects:

n.a.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 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	Netherlands: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	26
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

51 patients were screened, 40 were included

Period 1

Period 1 title	trial (overall period)
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	Lixisenatide

Arm description: -

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

Dosage and administration details:

once daily 20 mcg

Arm title	Glulisine

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	insulin glulisine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

once daily at breakfast, starting at 2 units - titration towards glucose 5-8 2-hr after breakfast

Number of subjects in period 1[1]	Lixisenatide	Glulisine
Started	20	19
Completed	17	18
Not completed	3	1
Adverse event, non-fatal	3	-
Protocol deviation	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One patient was included in the study, yet withdrew consent before randomisation

Baseline characteristics

Reporting groups	
Reporting group title	Lixisenatide
Reporting group description: -	
Reporting group title	Glulisine
Reporting group description: -	

Reporting group values	Lixisenatide	Glulisine	Total
Number of subjects	20	19	39
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			
geometric mean	62	61	
standard deviation	± 7	± 7	-
Gender categorical Units: Subjects			
Female	8	8	16
Male	12	11	23

End points

End points reporting groups	
Reporting group title	Lixisenatide
Reporting group description: -	
Reporting group title	Glulisine
Reporting group description: -	
Subject analysis set title	Kidney function
Subject analysis set type	Per protocol
Subject analysis set description: Kidney function	

Primary: Kidney function	
End point title	Kidney function
End point description:	
End point type	Primary
End point timeframe: full study	

End point values	Lixisenatide	Glulisine	Kidney function	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	17	18	35	
Units: 1				
geometric mean (standard error)	92 (± 4)	83 (± 5)	0.1 (± 0.1)	

Statistical analyses

Statistical analysis title	GFR
Comparison groups	Lixisenatide v Glulisine
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.989
Method	Regression, Linear

Adverse events

Adverse events information	
Timeframe for reporting adverse events: entire study	
Assessment type	Systematic

Dictionary used	
Dictionary name	no dictionary used
Dictionary version	0

Reporting groups	
Reporting group title	Glulisin
Reporting group description: -	
Reporting group title	Lixisenatide
Reporting group description: -	

Serious adverse events	Glulisin	Lixisenatide	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Atrial fibrillation	Additional description: one patient randomised to insulin glulisin experienced two episodes of (new-onset) symptomatic atrial fibrillation after the astart of the intervention. Patient recovered fully after hospital admision		
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Glulisin	Lixisenatide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 19 (68.42%)	11 / 20 (55.00%)	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	11 / 20 (55.00%)	
occurrences (all)	0	11	
Endocrine disorders			
Hypoglycaemia			

subjects affected / exposed occurrences (all)	13 / 19 (68.42%) 0	0 / 20 (0.00%) 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/30353743

http://www.ncbi.nlm.nih.gov/pubmed/29915021

http://www.ncbi.nlm.nih.gov/pubmed/29341461

http://www.ncbi.nlm.nih.gov/pubmed/28449402