Clinical trial results:
Effects of Linagliptin on Renal Endothelium Function in Patients with Type 2 Diabetes.

Summary

EudraCT number	2012-002278-30
Trial protocol	DE
Global end of trial date	06 February 2014

Results information

Result version number	v1 (current)
This version publication date	28 July 2021
First version publication date	28 July 2021

Trial information

Trial identification

Sponsor protocol code	CRC2012LINA

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Erlangen
Sponsor organisation address	Maximiliansplatz 2, Erlangen, Germany,
Public contact	Clinical Research Center, Clinical Research Center, Department of Nephrology and Hypertension, University of Erlangen-Nürnberg, 0049 91318536245, roland.schmieder@uk-erlangen.de
Scientific contact	Clinical Research Center, Clinical Research Center, Department of Nephrology and Hypertension, University of Erlangen-Nürnberg, 0049 91318536245, roland.schmieder@uk-erlangen.de

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	18 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2013
Global end of trial reached?	Yes
Global end of trial date	06 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of linagliptin compared to placebo on basal production and release of nitric oxide (NO) from renal vasculature, as assessed by changes of renal plasma flow due to L-NMMA infusion.

Protection of trial subjects:

Physical examinations, vital signs, checking concomitant medication, assessment of adverse events, measurement of safety laboratory markers (including glucose levels, biochemistry, haematology and urinanalsis) were done regularly in the course of the study.
Home blood glucose measurements (Home Blood Glucose Monitoring) were performed by the study participants during the whole duration of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 July 2012
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: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	53
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited via advertising in local newspapers, by our G.P. / local network in Erlangen/Nürnberg/Fürth and by our University Outpatient Clinic.
Participants were included after study physician has evaluated in- and exclusion criteria and after the participant has given his/her oral and written informed consent.

Pre-assignment

Screening details:

we screened female and male patients, aged between 18 and 70 years with type 2 diabetes, without diabetic nephropathy. Eligible patients entered a 4 week run-in/wash-out phase, if pretreated with any blood glucose lowering agent, or a 2 week run-in/wash-out phase, if not pretreated.

Period 1

Period 1 title	Treatment Period 1 (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?	No
Arm title	Linagliptin

Arm description:

The study followed randomized cross-over-design, i.e. subjects underwent both treatment arms in randomized order for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Linagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

5 mg once daily

Arm title	Placebo

Arm description:

This study followed randomized cross-over-design, e.e. subjects underwent both treatment arms in randomized order for 4 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

once daily

Number of subjects in period 1	Linagliptin	Placebo
Started	66	66
Completed	62	62
Not completed	4	4
Adverse event, non-fatal	3	3
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Period 1

Reporting group description: -

Reporting group values	Treatment Period 1	Total	
Number of subjects	66	66	
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)	53	53	
From 65-84 years	13	13	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	23	23	
Male	43	43	

End points

End points reporting groups

Reporting group title	Linagliptin
Reporting group description:	
The study followed randomized cross-over-design, i.e. subjects underwent both treatment arms in randomized order for 4 weeks.	
Reporting group title	Placebo
Reporting group description:	
This study followed randomized cross-over-design, e.e. subjects underwent both treatment arms in randomized order for 4 weeks	

Primary: Effect of Linagliptin compared to placebo by change of renal plasma flow due to L-NMMA infusion

End point title	Effect of Linagliptin compared to placebo by change of renal plasma flow due to L-NMMA infusion
End point description:	
End point type	Primary
End point timeframe:	
4 weeks	

End point values	Linagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	62		
Units: ml/min				
arithmetic mean (standard deviation)	-50.9 (± 34)	-54.2 (± 30)		

Statistical analyses

Statistical analysis title	effect of linagliptin on RPF compared to placebo
Comparison groups	Linagliptin v Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≤ 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	2.5

Secondary: Effect of Linagliptin compared to placebo on RPF

End point title	Effect of Linagliptin compared to placebo on RPF

End point description:

End point type	Secondary

End point timeframe:

4 weeks

End point values	Linagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	62		
Units: ml/min				
arithmetic mean (standard deviation)	612 (± 106)	621 (± 91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Effect of Linagliptin compared to placebo on GFR

End point title	Effect of Linagliptin compared to placebo on GFR

End point description:

End point type	Secondary

End point timeframe:

4 weeks

End point values	Linagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	62		
Units: ml/min				
arithmetic mean (standard deviation)	142 (± 16)	142 (± 15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Effect of Linagliptin compared to placebo on RVR (renal vessel resistance)

End point title	Effect of Linagliptin compared to placebo on RVR (renal vessel resistance)

End point description:

End point type	Secondary

End point timeframe:

4 weeks

End point values	Linagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	62		
Units: ml/min				
arithmetic mean (standard deviation)	88.4 (± 18)	92.1 (± 21)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

In the course of the intire study , each adverse event had to be reported on an Adverse Event Case Report Form as soon as known, in general at the subsequent study visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	all patients treated with IMP

Reporting group description: -

Serious adverse events	all patients treated with IMP		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 66 (1.52%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Erysipelas			
subjects affected / exposed	1 / 66 (1.52%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	all patients treated with IMP		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 66 (100.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 66 (28.79%)		
occurrences (all)	19		
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	3 / 66 (4.55%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 66 (7.58%)		
occurrences (all)	5		
Infections and infestations			
Cough			
subjects affected / exposed	4 / 66 (6.06%)		
occurrences (all)	4		
Cystitis			
subjects affected / exposed	3 / 66 (4.55%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	35 / 66 (53.03%)		
occurrences (all)	35		

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