Clinical trial results:
Effects of Linagliptin on Endothelial- , Renal-, and Retinal Function in Comparison to Placebo in Patients with Hypertension and Albuminuria

Summary

EudraCT number	2012-004300-35
Trial protocol	DE
Global end of trial date	30 September 2014

Results information

Result version number	v1 (current)
This version publication date	01 June 2022
First version publication date	01 June 2022

Trial information

Trial identification

Sponsor protocol code	ikfe-Lina-003

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Profil Mainz GmbH & Co. KG
Sponsor organisation address	Rheinstr. 4c, Mainz, Germany, 55116
Public contact	Contract Research Organisation, Clinlogix Europe GmbH, +49 61313279032, cforkel@clinlogix.de
Scientific contact	Contract Research Organisation, Clinlogix Europe GmbH, +49 61313279032, cforkel@clinlogix.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	22 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 September 2014
Global end of trial reached?	Yes
Global end of trial date	30 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to investigate the effect of Linagliptin in comparison to placebo on the urine albumin-to-creatinine ratio (UACR) in patients with high blood pressure and an increased albumin excretion.

Protection of trial subjects:

A patient will only be enrolled in the study after obtaining a written informed consent to participation. During patient information, the investigator must provide a complete explanation of the study (benefits, risks, rights and obligations) and check that the patient fulfills all of the inclusion criteria and none of the exclusion criteria

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 January 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: 43
Worldwide total number of subjects	43
EEA total number of subjects	43

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)	13
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment from own database and by advertisement (Germany)

Pre-assignment

Screening details:

- Arterial hypertension
- Stable antihypertensive treatment within the last 3 months
- Age ≥ 45 – ≤ 80 years
- Micro- or macroalbuminuria defined as UACR in morning urine > 20 mg/g in female and > 30 mg/g in male and/or arterial hypertension for more than 5 years

Period 1

Period 1 title	Overall 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	Placebo arm

Arm description:

once daily administration of Placebo

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

Dosage and administration details:

once daily

Arm title	Linagliptin arm

Arm description:

once daily administration of Linagliptin

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

Dosage and administration details:

5 mg once daily

Number of subjects in period 1	Placebo arm	Linagliptin arm
Started	22	21
Completed	22	21

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	43	43	
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	66.2		
standard deviation	± 6.6	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	33	33	
Height Units: centimetre			
arithmetic mean	171.9		
standard deviation	± 7.5	-	
Weight Units: kilogram(s)			
arithmetic mean	85.9		
standard deviation	± 15.2	-	
Waist circumference Units: centimetre			
arithmetic mean	99.0		
standard deviation	± 12.1	-	
Hip circumference Units: centimetre			
arithmetic mean	102.7		
standard deviation	± 15.3	-	
Systolic blood pressure Units: mmHg			
arithmetic mean	139.8		
standard deviation	± 12.8	-	

Diastolic blood pressure Units: mmHg			
arithmetic mean	79.7		
standard deviation	± 10.8	-	
Pulse rate Units: beats/min			
arithmetic mean	60.6		
standard deviation	± 10.1	-	

End points

End points reporting groups	
Reporting group title	Placebo arm
Reporting group description: once daily administration of Placebo	
Reporting group title	Linagliptin arm
Reporting group description: once daily administration of Linagliptin	

Primary: Comparison of urine albumin-to-creatinine ratio (UACR)	
End point title	Comparison of urine albumin-to-creatinine ratio (UACR)
End point description:	
End point type	Primary
End point timeframe: measurement on visit 2 and visit 5	

End point values	Placebo arm	Linagliptin arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	21		
Units: percent				
arithmetic mean (standard deviation)	21.2 (± 71.0)	47.6 (± 102.3)		

Statistical analyses

Statistical analysis title	UACR ratio / arm1:arm 2
Comparison groups	Placebo arm v Linagliptin arm
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall trial	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

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	1 / 43 (2.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Bite			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 43 (58.14%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod bite			

subjects affected / exposed occurrences (all) Post procedural discomfort subjects affected / exposed occurrences (all) Tooth fracture subjects affected / exposed occurrences (all) Radial head dislocation subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1 1 / 43 (2.33%) 1 1 / 43 (2.33%) 1 1 / 43 (2.33%) 1		
Vascular disorders Haematoma subjects affected / exposed occurrences (all)	 1 / 43 (2.33%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	 1 / 43 (2.33%) 1		
Eye disorders Eye allergy subjects affected / exposed occurrences (all)	 1 / 43 (2.33%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 1 / 43 (2.33%) 1 1 / 43 (2.33%) 1		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	 2 / 43 (4.65%) 2		
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Musculoskeletal stiffness			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Foot deformity			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Eczema infected			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	4 / 43 (9.30%)		
occurrences (all)	4		
Laryngitis			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		

Mastitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1 8 / 43 (18.60%) 8 2 / 43 (4.65%) 2		
Metabolism and nutrition disorders Gout subjects affected / exposed occurrences (all) Hypoglycaemia subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2 1 / 43 (2.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 June 2013	changes regarding two inclusion criteria

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported