Clinical trial results:
A randomised, double blind, placebo-controlled study of the effect of liraglutide on arterial blood pressure in hypertensive patients with type 2 diabetes mellitus

Summary

EudraCT number	2013-002348-99
Trial protocol	GR
Global end of trial date	19 July 2017

Results information

Result version number	v1 (current)
This version publication date	02 November 2018
First version publication date	02 November 2018

Trial information

Trial identification

Sponsor protocol code	AUTH88622

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1125-9028

Notes:

Sponsors

Sponsor organisation name	Aristotle University Thessaloniki
Sponsor organisation address	49 Konstantinoupoleos Street, Thessaloniki, Greece,
Public contact	Apostolos Tsapas, Second Medical Department, +30 2310992850, atsapas@auth.gr
Scientific contact	Apostolos Tsapas, Second Medical Department, +30 2310992850, atsapas@auth.gr

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	31 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 July 2017
Global end of trial reached?	Yes
Global end of trial date	19 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

A randomised, double blind, placebo-controlled study in patients with type 2 diabetes mellitus (T2DM), investigating the effect of liraglutide on blood pressure (BP), assessed by 24 h ambulatory blood pressure monitoring (ABPM).

Protection of trial subjects:

Written informed consent was obtained from all trial participants before study entry. The protocol was developed in line with the Declaration of Helsinki and was approved by all institutional review boards as well as the Greek national ethics committee. Subjects enrolled into the study were asked about potential adverse events at every contact with the study site.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 November 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	Greece: 62
Worldwide total number of subjects	62
EEA total number of subjects	62

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)	40
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

We included adults with inadequatelly controlled type 2 diabetes (HbA1c 7.0-10%) and pre-hypertension or stage 1 hypertension (based on JNC-7 criteria) on stable background atnihyperglycaemic and antihypertensive therapy for at least 12 and 6 weeks respectively prior to recruitement.

Period 1

Period 1 title	Active treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Liraglutide

Arm description: -

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

Dosage and administration details:

Once daily 0.6 mg titrated to 1.2 mg after the first week

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Once daily

Number of subjects in period 1	Liraglutide	Placebo
Started	31	31
Completed	29	29
Not completed	2	2
Consent withdrawn by subject	1	-
Adverse event, non-fatal	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Liraglutide
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Liraglutide	Placebo	Total
Number of subjects	31	31	62
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	60.5	59.9	
standard deviation	± 12.0	± 9.7	-
Gender categorical Units: Subjects			
Female	12	9	21
Male	19	22	41
Duration of diabetes Units: years			
median	8.0	10.0	
inter-quartile range (Q1-Q3)	5.0 to 11.0	6.0 to 14.0	-
Body weight Units: kg			
arithmetic mean	94.4	101.7	
standard deviation	± 14.8	± 21.9	-

End points

End points reporting groups	
Reporting group title	Liraglutide
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: 24-h systolic blood pressure

End point title	24-h systolic blood pressure
End point description:	
End point type	Primary
End point timeframe:	
Five weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: mmHg				
arithmetic mean (standard error)	-4.72 (± 1.43)	1.02 (± 1.43)		

Statistical analyses

Statistical analysis title	Analysis of covariance
Comparison groups	Liraglutide v Placebo
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA

Secondary: 24-h diastolic blood pressure

End point title	24-h diastolic blood pressure
End point description:	
End point type	Secondary
End point timeframe:	
Five weeks	

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: mmHg				
arithmetic mean (standard error)	-0.58 (± 0.99)	0.84 (± 0.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: 24-h heart rate

End point title	24-h heart rate

End point description:

End point type	Secondary

End point timeframe:

Five weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: beats/min				
arithmetic mean (standard error)	8.55 (± 1.03)	2.39 (± 1.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: Daytime systolic blood pressure

End point title	Daytime systolic blood pressure

End point description:

End point type	Secondary

End point timeframe:

Five weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: mmHg				
arithmetic mean (standard error)	-5.61 (± 1.47)	0.83 (± 1.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Daytime diastolic blood pressure

End point title	Daytime diastolic blood pressure

End point description:

End point type	Secondary

End point timeframe:

Five weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: mmHg				
arithmetic mean (standard error)	-1.10 (± 1.02)	0.60 (± 1.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: Daytime heart rate

End point title	Daytime heart rate

End point description:

End point type	Secondary

End point timeframe:

Five weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: beats/min				
arithmetic mean (standard error)	8.35 (± 1.06)	2.16 (± 1.06)		

Statistical analyses

No statistical analyses for this end point

Secondary: Nighttime systolic blood pressure

End point title	Nighttime systolic blood pressure

End point description:

End point type	Secondary

End point timeframe:

Five weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: mmHg				
arithmetic mean (standard error)	-1.67 (± 1.65)	1.77 (± 1.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Nighttime diastolic blood pressure

End point title	Nighttime diastolic blood pressure

End point description:

End point type	Secondary

End point timeframe:

Five weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: mmHg				
arithmetic mean (standard error)	-0.30 (± 1.07)	0.67 (± 1.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: Nighttime heart rate

End point title	Nighttime heart rate

End point description:

End point type	Secondary

End point timeframe:

Five weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: beats/min				
arithmetic mean (standard error)	9.25 (± 1.11)	3.09 (± 1.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Sodium excretion

End point title	Sodium excretion

End point description:

End point type	Secondary

End point timeframe:

Five weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: mmol/24-h				
arithmetic mean (standard error)	-16.86 (± 14.93)	-13.93 (± 14.93)		

Statistical analyses

No statistical analyses for this end point

Secondary: Lithium excretion at endpoint

End point title	Lithium excretion at endpoint

End point description:

End point type	Secondary

End point timeframe:

Five weeks

End point values	Liraglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: mg/24-h				
arithmetic mean (standard error)	3.71 (± 20.20)	-7.21 (± 40.53)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Active treatment	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	19
Reporting groups	
Reporting group title	Liraglutide
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Liraglutide	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)	0 / 31 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Liraglutide	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 31 (12.90%)	4 / 31 (12.90%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 31 (3.23%)	1 / 31 (3.23%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Dizziness			
subjects affected / exposed	2 / 31 (6.45%)	0 / 31 (0.00%)	
occurrences (all)	1	1	
Generalised rash			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	

Injection-site rash			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 31 (3.23%)	1 / 31 (3.23%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	2 / 31 (6.45%)	1 / 31 (3.23%)	
occurrences (all)	2	1	
Constipation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 September 2016	Lower haemoglobin A1c threshold for inclusion changed to 7.0%, lower estimated glomerular filtration rate threshold for inclusion changed to 30 ml/min, 24-h arterial blood pressure monitoring quality control criteria revised, end of trial date changed to 31-Aug-2017
29 September 2016	Four new trial sites included

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported