Clinical trial results:
The effect of glucagon-like-peptide 1 (GLP-1) analogues on inflammation in humans with diabetic kidney disease.

Summary

EudraCT number	2012-005482-12
Trial protocol	IE
Global end of trial date	01 November 2015

Results information

Result version number	v1 (current)
This version publication date	07 December 2018
First version publication date	07 December 2018
Summary attachment (see zip file)	Summary (Screen Shot 2018-11-17 at 15.34.00.png)

Trial information

Trial identification

Sponsor protocol code	GLP-1-2012-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01847313
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University College Dublin
Sponsor organisation address	Belfield, Dublin, Ireland,
Public contact	Karl Neff, UCD Clinical Research Centre, St Vincent's University Hospital, karljneff@gmail.com
Scientific contact	Karl Neff, UCD Clinical Research Centre, St Vincent's University Hospital, karljneff@gmail.com

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	09 November 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 November 2015
Global end of trial reached?	Yes
Global end of trial date	01 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective:
The primary objective of this study is to compare the change in pro-inflammatory cytokine monocyte-chemotactic protein 1 (MCP-1) in urine in subjects treated with liraglutide over a 26 week treatment period versus a matched control group who received no liraglutide.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Ireland: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	8
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All subjects recruited within the Diabetes Clinics of St Vincent's Healthcare Group in line with inclusion and exclusion criteria as listed below.

Pre-assignment

Screening details:

Criteria: Inclusion Criteria:
• Type 2 diabetes with a HbA1c of 42-75mmol/mol (6-9%DCCT)
• Male or female aged above 30 years
• Have a negative pregnancy test at screening (women of child bearing potential only)
• Body mass index (BMI) of 25kg/m2 or greater
• On a renin-angiotensin system antagonist, at a stable dose, for at least 8 weeks befo

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard Care and Liraglutide

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	
Other name	Glucagon like peptide 1 receptor agonist, NN2211
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

0.6 mg daily

Arm title	Standard Care alone

Arm description: -

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Standard Care and Liraglutide	Standard Care alone
Started	10	10
Completed	10	10

Period 2	
Period 2 title	End of Study
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded
Blinding implementation details: Not blinded	

Arms	
Are arms mutually exclusive?	Yes
Arm title	Standard Care and Liraglutide
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	
Other name	Glucagon like peptide 1 receptor agonist, NN2211
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 0.6 mg daily	
Arm title	Standard Care alone
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Standard Care and Liraglutide	Standard Care alone
Started	10	10
Completed	10	8
Not completed	0	2
Adverse event, serious fatal	-	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	20	20	
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)	8	8	
From 65-84 years	12	12	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	65		
standard deviation	± 9	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	14	14	
Urinary Albumin Excretion Rate Units: ug/ml			
arithmetic mean	106.9		
standard deviation	± 109	-	
MCP-1:Creatinine Ratio in Urine Units: ng/mmol			
arithmetic mean	27.2		
standard deviation	± 19.6	-	
sCD163:creatinine ratio in urine Units: pg/mmol			
arithmetic mean	44		
standard deviation	± 51	-	
sCD163 in serum Units: ng/ml			
arithmetic mean	100		
standard deviation	± 45	-	

End points

End points reporting groups

Reporting group title	Standard Care and Liraglutide
Reporting group description: -	
Reporting group title	Standard Care alone
Reporting group description: -	
Reporting group title	Standard Care and Liraglutide
Reporting group description: -	
Reporting group title	Standard Care alone
Reporting group description: -	

Primary: Urinary MCP1:Creatinine ratio

End point title	Urinary MCP1:Creatinine ratio[1]
End point description:	
End point type	Primary
End point timeframe:	
Six months	

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: As per our statistical plan, we tested for significance between baseline and end of study in both groups. There was no significant difference and therefore further statistical analysis was not completed.

Urinary MCP-1 creatinine ratios did not change from baseline to 26 weeks in either Standard Therapy (p=0.33) or liraglutide groups (p=0.46). There was no difference in urinary MCP-1 between groups at baseline (p=0.21) or at 26 weeks (p=0.55).

End point values	Standard Care and Liraglutide	Standard Care alone	Standard Care and Liraglutide	Standard Care alone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	8	9	8
Units: ng/mmol				
arithmetic mean (standard deviation)	32.8 (± 25.7)	20.8 (± 6.0)	27.9 (± 14.3)	24.3 (± 15.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Urine Albumin Excretion Rate

End point title	Urine Albumin Excretion Rate
End point description:	
End point type	Secondary
End point timeframe:	
Six months	

End point values	Standard Care and Liraglutide	Standard Care alone	Standard Care and Liraglutide	Standard Care alone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	9	7
Units: ug/min				
arithmetic mean (standard deviation)	106.9 (± 109.5)	122.8 (± 142.1)	144.1 (± 232.6)	132.4 (± 101.3)

Statistical analyses

No statistical analyses for this end point

Secondary: sCD163 in Serum

End point title	sCD163 in Serum

End point description:

End point type	Secondary

End point timeframe:

Six months

End point values	Standard Care and Liraglutide	Standard Care alone	Standard Care and Liraglutide	Standard Care alone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	8	10	8
Units: ng/ml				
arithmetic mean (standard deviation)	98 (± 45)	106 (± 47)	82 (± 34)	84 (± 23)

Statistical analyses

No statistical analyses for this end point

Secondary: sCD163:creatinine ratio in urine

End point title	sCD163:creatinine ratio in urine

End point description:

End point type	Secondary

End point timeframe:

Six months

End point values	Standard Care and Liraglutide	Standard Care alone	Standard Care and Liraglutide	Standard Care alone
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	8	10	8
Units: pg/mmol				
arithmetic mean (standard deviation)	51 (± 60)	37 (± 38)	27.9 (± 14.0)	24.3 (± 14.4)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Starting from the first administration of the IMP through to the End of Study Visit (30 weeks) all Adverse Event and Serious Adverse event information was collected at each visit.

Adverse event reporting additional description:

AEs were collected by the PI and Sub-investigators and recorded in the CRF/site file/medical record. AEs/ SAEs were recorded in the CRF module for AE in verbatim terms. In case of several signs/symptoms, a single syndrome or diagnosis was recorded. In the event of an AE, investigators adjudicated whether the AE was serious, the start date, the stop

Assessment type	Non-systematic

Dictionary used

Dictionary name	NA
Dictionary version	NA

Reporting groups

Reporting group title	Standard Care alone
Reporting group description: -	
Reporting group title	Standard Care with Liraglutide

Reporting group description: -

Serious adverse events	Standard Care alone	Standard Care with Liraglutide	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Cardiac disorders			
Heart failure			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Paroxysmal atrial fibrillation			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
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: 0 %

Non-serious adverse events	Standard Care alone	Standard Care with Liraglutide	
Total subjects affected by non-serious adverse events subjects affected / exposed	7 / 10 (70.00%)	8 / 10 (80.00%)	
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Blood and lymphatic system disorders Hypokalaemia subjects affected / exposed occurrences (all) Hyponatraemia subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2 0 / 10 (0.00%) 0	0 / 10 (0.00%) 0 1 / 10 (10.00%) 1	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Loose stool subjects affected / exposed occurrences (all) Mouth ulceration subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 1 / 10 (10.00%) 1	2 / 10 (20.00%) 2 1 / 10 (10.00%) 1 2 / 10 (20.00%) 2 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0	
Reproductive system and breast disorders			

Erectile dysfunction			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Ingrown toenail			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Viral illness			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	
occurrences (all)	1	2	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Nil

Notes: