Clinical trial results:
The effects of GLP-1 in Maturity- onset diabetes of the young (MODY)

Summary

EudraCT number	2012-000592-17
Trial protocol	DK
Global end of trial date	23 August 2013

Results information

Result version number	v1 (current)
This version publication date	03 December 2021
First version publication date	03 December 2021

Trial information

Trial identification

Sponsor protocol code	MODY-TREAT

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01610934
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Diabetes Research Division
Sponsor organisation address	Niels Andersens vej , Gentofte, Denmark, 2820
Public contact	Clinical trials information, Signe H. Østoft, Diabetes Research Division, +45 21230343, s.ostoft@dadlnet.dk
Scientific contact	Clinical trials information, Signe H. Østoft, Diabetes Research Division, +45 21230343, s.ostoft@dadlnet.dk

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	23 August 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 August 2013
Global end of trial reached?	Yes
Global end of trial date	23 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the study is to investigate long term (6 weeks) effects of liraglutide compared to glimepiride on Fasting Plasma Glucose in patients with MODY3 in a double-blind, randomised cross-over trial.

Protection of trial subjects:

No specific measures, besides blood glucose monitoring.

Background therapy: -

Evidence for comparator:

Glimepiride was at that time standard treatment for MODY patients, but with high risk of hypoglycaemia. Liraglutide (GLP-1 RA) was chosen due to low risk of hypoglycaemia.

Actual start date of recruitment	01 August 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	Denmark: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited in the period of Aug 2012-May 2013. All patients recruited in Denmark.

Pre-assignment

Screening details:

Patients were screened at a pre-treatment evaluation according to in- and exclusion criteria. Eligible pt's had 1 week wash-out before starting trial medication. Cross-over design with 2 weeks washout efore corssing over.

Period 1

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

Blinding implementation details:

Double blinded double dummy cross-over design. Glimepiride covered in capsules and liraglutide with placebo from company. Unblinding only after data analysis.

Arms

Are arms mutually exclusive?	No
Arm title	Sulphonylurea (SU)

Arm description:

Pt's treated with glimepiride (SU)

Arm type	Active comparator
Investigational medicinal product name	glimepiride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dose according to blood glucose response (Titration). Glimepiride/placebo is administered orally (glimepirid, tablet ½ mg and 1 mg).

Arm title	GLP-1 RA

Arm description:

Pt's treated with liraglutide (GLP-1 RA)

Arm type	Experimental
Investigational medicinal product name	liraglutide
Investigational medicinal product code	
Other name	Victoza
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Victoza®/placebo is administered subcutaneously one time daily in the entire treatment period (Day 8-49/57-98) and up-titrated as follows: Day8--14/5763: 0.6 mg Victoza®/placebo; Day 15--21/64--70: 1.2mg Victoza/placebo; Day 22--49/71--98: 1.8 mg Victoza®/placebo). Patients who, due to adverse events, do not tolerate up-titration to1.8 mg liraglutide will remain on 1.2 mg of liraglutide. The patients are instructed in injection technique.

Arm title	Baseline

Arm description:

16 patients entered the baseline period before being randomised to SU or GLP-1RA in a cross-over design.

Arm type	Baseline

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Sulphonylurea (SU)	GLP-1 RA	Baseline
Started	15	15	15
Completed	15	15	15

Baseline characteristics

Reporting groups	
Reporting group title	Full trial

Reporting group description:

16 patients entered a cross-over study, being their own control. One patient dropped out due to side effects to liraglutide (vomiting/diarrhea). Therefore data is reported on 15 patients in cross-over design (30 in total)

Reporting group values	Full trial	Total	
Number of subjects	15	15	
Age categorical Units: Subjects			
Adults (18-64 years)	13	13	
From 65-84 years	2	2	
Age continuous Units: years			
log mean	38.9		
standard deviation	± 16.3	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	8	8	

End points

End points reporting groups

Reporting group title	Sulphonylurea (SU)
Reporting group description: Pt's treated with glimepiride (SU)	
Reporting group title	GLP-1 RA
Reporting group description: Pt's treated with liraglutide (GLP-1 RA)	
Reporting group title	Baseline
Reporting group description: 16 patients entered the baseline period before being randomised to SU or GLP-1RA in a cross-over design.	

Primary: Fasting PLasma Glucose (FPG)

End point title	Fasting PLasma Glucose (FPG)
End point description:	
End point type	Primary
End point timeframe: FPG was meassured at 3 clinic visists: at baseline, and in the end of each treatment period (after 6 weeks treatment with glimepiride and liraglutide resp.)	

End point values	Sulphonylurea (SU)	GLP-1 RA	Baseline	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15[1]	15[2]	15	
Units: mmol/L				
log mean (standard error)	7.2 (± 0.6)	8.2 (± 0.8)	9.9 (± 0.8)	

Notes:

[1] - 16 subj were treated with glimepiride. 1 subj withdrew on liraglutide. Data reported on 15 subj.

[2] - 16 subj were treated with glimepiride. 1 subj withdrew on liraglutide. Data reported on 15 subj.

Attachments (see zip file)	Publication MODY-TREAT/Dia Care-2014-Østoft-1797-805.pdf MODY-TREAT protocol/MODY-TREAT_protokol-vs-2.0.pdf MODY-TREAT Plasma Glucose/MODY-TREAT Plasma glucose BL

Statistical analyses

Statistical analysis title	Linear mixed-effect modeling
Statistical analysis description: Linear mixed-effect modeling was used for analysis of repeated measures using R statistical software. Data were transformed according to distribution pattern. A "top-down" modeling strategy, with family identity as random variable, was used. A homogeneous or heterogeneous residual variance structure was chosen according to likelihood ratios. Bonferroni adjustments were used as post hoc analysis. Values are expressed as mean +/- SEM.	
Comparison groups	Sulphonylurea (SU) v GLP-1 RA

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	< 0.05 [4]
Method	ANOVA
Parameter estimate	Mean difference (final values)

Notes:

[3] - Each treatment was compared with baseline, and not with eachother, from repeated-measures ANOVA for variations between treatments and baseline.
[4] - Differences resulting in P-values < 0.05 were considered significant.

Secondary: Fructosamine

End point title	Fructosamine

End point description:

End point type	Secondary

End point timeframe:

Fructosamine was measured 3 times: at baseline and in the end of each treatment period (glimepiride and liraglutide respectively)

End point values	Sulphonylurea (SU)	GLP-1 RA	Baseline	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	15	15	
Units: micromole(s)/litre				
log mean (standard error)	273 (± 14)	296 (± 20)	294 (± 16)	

Attachments (see zip file)	MODY-TREAT Fructosamine BL Glime Lira_EuDraCT.xlsx

Statistical analyses

Statistical analysis title	Linear mixed-effect modelling

Statistical analysis description:

Linear mixed-effect modeling was used for analysis of repeated measures using R statistical software. Data were transformed according to distribution pattern. A “top-down” modeling strategy, with family identity as random variable, was used. A homogeneous or heterogeneous residual variance structure was chosen according to likelihood ratios. Bonferroni adjustments were used as post hoc analysis. Values are expressed as mean +/- SEM.

Comparison groups	Sulphonylurea (SU) v GLP-1 RA
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	< 0.05 [6]
Method	ANOVA

Notes:

[5] - Each treatment was compared with baseline, and not with eachother, from repeated-measures ANOVA for variations between treatments and baseline.
[6] - P-values <0.05 were considered significant.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE's were assessed in the full trial period from Aug-01-2012 to Aug-23-2013.

Adverse event reporting additional description:

A total of 23 AEs were reported, consisting of primarily events of hypoglycaemia (19 reports). Other reported events: Tiredness (1 report), reduced appetite (2 reports), heartburn (1 report), nausea (1 report) and vomiting/diarrhea (1 report).
All the reported AEs were estimated as related to the study.

Assessment type	Systematic

Dictionary used

Dictionary name	Local hospital
Dictionary version	1

Reporting groups

Reporting group title	Glimepiride
Reporting group description: -	
Reporting group title	liraglutide

Reporting group description: -

Serious adverse events	Glimepiride	liraglutide	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Glimepiride	liraglutide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 15 (66.67%)	1 / 15 (6.67%)	
Endocrine disorders			
Hypoglycaemia	Additional description: Totally 19 events of hypoglycaemia were reported. All were mild. 17 events with BG 3.2-3.9 mM; 2 events with BG 2.0-3.0 mM. 3 episodes in 1 patient on liraglutide. 16 events in patients on glimepiride.		
subjects affected / exposed	10 / 15 (66.67%)	1 / 15 (6.67%)	
occurrences (all)	16	3	

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.

None

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24929431

http://www.ncbi.nlm.nih.gov/pubmed/25953829

http://www.ncbi.nlm.nih.gov/pubmed/24677712

http://www.ncbi.nlm.nih.gov/pubmed/26324089

http://www.ncbi.nlm.nih.gov/pubmed/14575972