

**Clinical trial results:****The Effect of Sitagliptin on Glucagon Dynamics and Incretin Hormones During Mild Hypoglycemia in Elderly Patients with Metformin-Treated Type 2 Diabetes****Summary**

EudraCT number	2014-002685-70
Trial protocol	SE
Global end of trial date	13 March 2018

Results information

Result version number	v1 (current)
This version publication date	10 March 2021
First version publication date	10 March 2021
Summary attachment (see zip file)	2014-002685-70 Results (EudraCT 2014-002685-70 results.pdf)

Trial information**Trial identification**

Sponsor protocol code	300A
-----------------------	------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02256189
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Lund university
Sponsor organisation address	Sölvegatan 19, Lund, Sweden, 22184
Public contact	Bo Ahrén, Lund university, 46 462220758, Bo.Ahren@med.lu.se
Scientific contact	Bo Ahrén, Lund university, 46 462220758, Bo.Ahren@med.lu.se

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	15 November 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 November 2017
Global end of trial reached?	Yes
Global end of trial date	13 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess if sitagliptin can improve the glucagon secretory response to mild hypoglycemia in elderly patients with metformin-treated type 2 diabetes.

Protection of trial subjects:

Subjects with type 2 diabetes

Background therapy:

Metformin

Evidence for comparator:

Sitagliptin versus placebo

Actual start date of recruitment	15 December 2014
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	Sweden: 28
Worldwide total number of subjects	28
EEA total number of subjects	28

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)	0
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

28 subjects were recruited through hospitals

Pre-assignment

Screening details:

Subjects were examined by physician and lab tests were taken

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	Investigator, Monitor, Data analyst, Subject

Blinding implementation details:

Patients received sitagliptin or placebo first, then placebo or sitagliptin. Randomization and blinding were handled by the University hospital pharmacist.

Arms

Are arms mutually exclusive?	Yes
Arm title	Sitagliptin

Arm description:

Sitagliptin 100mg once daily for four weeks followed by a hyperinsulinaemic hypoglycaemic clamp. Thereafter a 4 weeks wash out period followed by placebo treatment for 4 weeks followed by a hypoglycaemic clamp.

Arm type	Active comparator
Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg once daily

Arm title	Placebo
------------------	---------

Arm description:

Placebo treatment for four weeks followed by a hyperinsulinaemic hypoglycaemic clamp. Thereafter a 4 weeks wash out period followed by treatment with sitagliptin 100 mg daily for four weeks followed by a hypoglycaemic clamp.

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

Dosage and administration details:

One placebo tablet Daily for four weeks

Number of subjects in period 1	Sitagliptin	Placebo
Started	15	13
Completed	15	13

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
-----------------------	---------------

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	28	28	
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)	0	0	
From 65-84 years	28	28	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	73.6		
standard deviation	± 5.9	-	
Gender categorical			
Units: Subjects			
Female	11	11	
Male	17	17	
HbA1c			
Units: mmol/mol			
arithmetic mean	51.5		
standard deviation	± 7.2	-	
BMI			
Units: kg/m2			
arithmetic mean	30.2		
standard deviation	± 4.7	-	
Diabetes duration			
Units: years			
arithmetic mean	9.2		
standard deviation	± 6.6	-	

End points

End points reporting groups

Reporting group title	Sitagliptin
Reporting group description:	Sitagliptin 100mg once daily for four weeks followed by a hyperinsulinaemic hypoglycaemic clamp. Thereafter a 4 weeks wash out period followed by placebo treatment for 4 weeks followed by a hypoglycaemic clamp.
Reporting group title	Placebo
Reporting group description:	Placebo treatment for four weeks followed by a hyperinsulinaemic hypoglycaemic clamp. Thereafter a 4 weeks wash out period followed by treatment with sitagliptin 100 mg daily for four weeks followed by a hypoglycaemic clamp.

Primary: Glucagon levels at 3.5 mmol/L glucose during hypoglycaemic clamp

End point title	Glucagon levels at 3.5 mmol/L glucose during hypoglycaemic clamp
End point description:	
End point type	Primary
End point timeframe:	30 min after start of hypoglycaemia clamp

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: pmol/L				
arithmetic mean (standard error)	27.2 (± 1.7)	32.2 (± 2.1)		

Statistical analyses

Statistical analysis title	t-test
Comparison groups	Sitagliptin v Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	t-test, 2-sided

Primary: Glucagon levels at 3.1 mmol/L glucose during hypoglycaemic clamp

End point title	Glucagon levels at 3.1 mmol/L glucose during hypoglycaemic clamp
-----------------	--

End point description:

End point type Primary

End point timeframe:

60 min after start of hypoglycaemia clamp

End point values	Sitagliptin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	13		
Units: pmol/L				
arithmetic mean (standard error)	41.7 (\pm 3.4)	43.2 (\pm 2.2)		

Statistical analyses

Statistical analysis title	t-test
Comparison groups	Sitagliptin v Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.18
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Four weeks

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	21
--------------------	----

Reporting groups

Reporting group title	Sitagliptin
-----------------------	-------------

Reporting group description: -

Reporting group title	Placebo
-----------------------	---------

Reporting group description: -

Serious adverse events	Sitagliptin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (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: 5 %

Non-serious adverse events	Sitagliptin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 14 (35.71%)	5 / 14 (35.71%)	
Musculoskeletal and connective tissue disorders			
Joint stiffness			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Infections and infestations			
Common cold			
subjects affected / exposed	4 / 14 (28.57%)	4 / 14 (28.57%)	
occurrences (all)	4	4	

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

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29645341>