Clinical trial results:
Pasireotide in the treatment of hypoglycemia following gastric bypass surgery

Summary

EudraCT number	2018-001067-23
Trial protocol	DK
Global end of trial date	13 August 2018

Results information

Result version number	v1 (current)
This version publication date	13 May 2020
First version publication date	13 May 2020

Trial information

Trial identification

Sponsor protocol code	PasHypo

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03514576
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Urd Lynge Kielgast
Sponsor organisation address	Lykkebækvej 1, Køge, Denmark, 4600
Public contact	Caroline Christfort Øhrstrøm, Zealand University Hospital, 45 60625505, cacg@regionsjaelland.dk
Scientific contact	Caroline Christfort Øhrstrøm, Zealand University Hospital, 45 60625505, cacg@regionsjaelland.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	01 October 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effects of both 75 ug pasireotide (P75) and 150 ug pasireotide (P150) on the postprandial blood glucose response in RYGB operated patients with hypoglycemia.

Protection of trial subjects:

Subjects were asked to rest in a hospital bed during the mixed meal test. The intravenous catheter was inserted by a trained physician in order to minimise injection related pain and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2018
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: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited based on prior participation in the clinical trial HypoGB2015 (EudraCT number 2015-001086-50)

Pre-assignment

Screening details:

Medical assessment.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Baseline

Arm description:

Participants underwent a mixed meal tolerance test without prior treatment.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Pasireotide 75

Arm description:

Participants underwent a mixed meal tolerance test preceded by an injection of 75 ug pasireotide.

Arm type	Experimental
Investigational medicinal product name	pasireotide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A 75 ug gram dose was administered as a subcutaneous injection 30 minutes prior to the mixed meal test.

Arm title	Pasireotide 150

Arm description:

Participants underwent a mixed meal tolerance test preceded by an injection of 150 ug pasireotide.

Arm type	Experimental
Investigational medicinal product name	pasireotide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A 150 ug dose was administered as a subcutanous injection 30 minutes prior to the mixed meal test.

Arm title	Pasireotide 300

Arm description:

Participants underwent a mixed meal tolerance test preceded by an injection of 300 ug pasireotide.

Arm type	Experimental

Investigational medicinal product name	pasireotide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A dose of 300 ug was administered as a subcutanous injection 30 minutes prior to the mixed meal test

Number of subjects in period 1	Baseline	Pasireotide 75	Pasireotide 150
Started	5	5	5
Completed	5	5	5

Number of subjects in period 1	Pasireotide 300
Started	5
Completed	5

Baseline characteristics

Reporting groups	
Reporting group title	Baseline
Reporting group description:	
Participants underwent a mixed meal tolerance test without prior treatment.	
Reporting group title	Pasireotide 75
Reporting group description:	
Participants underwent a mixed meal tolerance test preceded by an injection of 75 ug pasireotide.	
Reporting group title	Pasireotide 150
Reporting group description:	
Participants underwent a mixed meal tolerance test preceded by an injection of 150 ug pasireotide.	
Reporting group title	Pasireotide 300
Reporting group description:	
Participants underwent a mixed meal tolerance test preceded by an injection of 300 ug pasireotide.	

Reporting group values	Baseline	Pasireotide 75	Pasireotide 150
Number of subjects	5	5	5
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	5	5
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	43	45	45
inter-quartile range (Q1-Q3)	32 to 57	34 to 59	34 to 59
Gender categorical Units: Subjects			
Female	5	5	5
Male	0	0	0

Reporting group values	Pasireotide 300	Total	
Number of subjects	5	5	
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)	5	5	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
median	43		
inter-quartile range (Q1-Q3)	32 to 57	-	
Gender categorical			
Units: Subjects			
Female	5	5	
Male	0	0	

End points

End points reporting groups	
Reporting group title	Baseline
Reporting group description:	
Participants underwent a mixed meal tolerance test without prior treatment.	
Reporting group title	Pasireotide 75
Reporting group description:	
Participants underwent a mixed meal tolerance test preceded by an injection of 75 ug pasireotide.	
Reporting group title	Pasireotide 150
Reporting group description:	
Participants underwent a mixed meal tolerance test preceded by an injection of 150 ug pasireotide.	
Reporting group title	Pasireotide 300
Reporting group description:	
Participants underwent a mixed meal tolerance test preceded by an injection of 300 ug pasireotide.	

Primary: Nadir glucose	
End point title	Nadir glucose
End point description:	
End point type	Primary
End point timeframe:	
Nadir blood glucose concentration during a 3-hour mixed meal tolerance test	

End point values	Baseline	Pasireotide 75	Pasireotide 150	Pasireotide 300
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	5
Units: mmol/l				
median (inter-quartile range (Q1-Q3))	3.4 (3.3 to 3.5)	6.2 (6 to 6.4)	8.1 (7.3 to 8.4)	8.9 (8.3 to 9.4)

Statistical analyses

Statistical analysis title	Friedmann's test
Comparison groups	Baseline v Pasireotide 75 v Pasireotide 150 v Pasireotide 300
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Friedmann's test

Secondary: Peak glucose

End point title	Peak glucose

End point description:

End point type	Secondary

End point timeframe:

Peak blood glucose concentration during a 3-hour mixed meal tolerance test with and without prior pasireotide administration

End point values	Baseline	Pasireotide 75	Pasireotide 150	Pasireotide 300
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	5
Units: mmol/l				
median (inter-quartile range (Q1-Q3))	10.7 (10.2 to 10.8)	14.1 (12.1 to 16.7)	15.2 (14.9 to 16.9)	14.4 (13.2 to 15.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Time in hypoglycemia

End point title	Time in hypoglycemia

End point description:

End point type	Secondary

End point timeframe:

Time spent with blood glucose values <3.9 mmol/l during a 3-hour mixed meal tolerance test with and without prior pasireotide administration

End point values	Baseline	Pasireotide 75	Pasireotide 150	Pasireotide 300
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	5
Units: minutes				
median (inter-quartile range (Q1-Q3))	38.3 (30 to 45.3)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)

Statistical analyses

No statistical analyses for this end point

Secondary: Time in hyperglycemia

End point title	Time in hyperglycemia

End point description:

End point type	Secondary

End point timeframe:

Time spent with blood glucose values >7.8 mmol/l during a 3-hour mixed meal tolerance test with and without prior pasireotide administration

End point values	Baseline	Pasireotide 75	Pasireotide 150	Pasireotide 300
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	5
Units: minutes				
median (inter-quartile range (Q1-Q3))	36.9 (25.2 to 37)	135.6 (127.3 to 137.3)	171.8 (168.5 to 175)	175 (172.2 to 176.9)

Statistical analyses

No statistical analyses for this end point

Secondary: iAUC glucose

End point title	iAUC glucose

End point description:

End point type	Secondary

End point timeframe:

Incremental area under the curve for blood glucose during a 3-hour mixed meal tolerance test with and without prior pasireotide administration

End point values	Baseline	Pasireotide 75	Pasireotide 150	Pasireotide 300
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	5
Units: mmol/L*min				
median (inter-quartile range (Q1-Q3))	308 (292 to 308)	706 (659 to 727)	853 (743 to 928)	958 (893 to 1054)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: iAUC insulin

End point title	iAUC insulin

End point description:

End point type	Other pre-specified

End point timeframe:

Incremental area under the curve for plasma insulin during a 3-hour mixed meal tolerance test with and without prior pasireotide administration

End point values	Baseline	Pasireotide 75	Pasireotide 150	Pasireotide 300
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	5
Units: pmol/l x min				
median (inter-quartile range (Q1-Q3))	49109 (40941 to 49388)	21750 (12988 to 27317)	21212 (19796 to 28426)	16635 (12678 to 17676)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: iAUC C-peptide

End point title	iAUC C-peptide

End point description:

End point type	Other pre-specified

End point timeframe:

Incremental area under the curve for plasma C-peptide during a 3-hour mixed meal tolerance test with and without prior pasireotide administration

End point values	Baseline	Pasireotide 75	Pasireotide 150	Pasireotide 300
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	5
Units: nmol/l x min				
median (inter-quartile range (Q1-Q3))	220 (218 to 250)	178 (133 to 218)	166 (97 to 209)	105 (95 to 118)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: iAUC GLP-1

End point title	iAUC GLP-1

End point description:

End point type	Other pre-specified

End point timeframe:

Incremental area under the curve for plasma GLP-1 (glucagon-like peptide 1) during a 3-hour mixed meal tolerance test with and without prior pasireotide administration

End point values	Baseline	Pasireotide 75	Pasireotide 150	Pasireotide 300
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	5
Units: pmol/l x min				
median (inter-quartile range (Q1-Q3))	4293 (4169 to 5288)	2173 (1730 to 4410)	2025 (1443 to 3215)	1144 (686 to 1296)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: During the 3 mixed meal tolerance test (3 hours) that were preceded by pasireotide administration.	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0
Reporting groups	
Reporting group title	Pasireotide 75
Reporting group description: Participants received a 75 ug pasireotide injection 30 minutes prior to a mixed meal tolerance test.	
Reporting group title	Pasireotide 150
Reporting group description: Participants received a 150 ug pasireotide injection 30 minutes prior to a mixed meal tolerance test.	
Reporting group title	Pasireotide 300
Reporting group description: Participants received a 300 ug pasireotide injection 30 minutes prior to a mixed meal tolerance test.	

Serious adverse events	Pasireotide 75	Pasireotide 150	Pasireotide 300
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Pasireotide 75	Pasireotide 150	Pasireotide 300
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
Cardiac disorders			
hypotension	Additional description: Hypotension and sweating.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

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.

The mixed meal tolerance tests with the 75 ug and the 150 ug pasireotide dose were performed 2.2 years after the baseline and the 300 ug pasireotide mixed meal tolerance tests.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31709494