Clinical trial results:
Ready-to-use dasiglucagon for the treatment of postprandial hypoglycaemia in Roux-en-Y gastric bypass operated patients

Summary

EudraCT number	2020-005241-16
Trial protocol	DK
Global end of trial date	12 June 2022

Results information

Result version number	v1 (current)
This version publication date	27 September 2023
First version publication date	27 September 2023

Trial information

Trial identification

Sponsor protocol code	CKN-DASI120-RYGB

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03984370
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Center for Clinical Metabolic Research at Gentofte Hospital
Sponsor organisation address	Gentofte Hospitalsvej 7, hall 7, 3rd floor, Hellerup, Denmark, 2900
Public contact	Herlev-Gentofte Hospital, Center for Clinical Metabolic Research at Gentofte Hospital, +45 60117434, casper.kjaersgaard.nielsen@regionh.dk
Scientific contact	Herlev-Gentofte Hospital, Center for Clinical Metabolic Research at Gentofte Hospital, 60117434 60117434, casper.kjaersgaard.nielsen@regionh.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	30 August 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 June 2022
Global end of trial reached?	Yes
Global end of trial date	12 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary aim of the study is to compare the effects of self-administered 120 µg dasiglucagon versus placebo (during postprandial hypoglycaemia) on CGM-assessed time spent in hypoglycaemia in RYGB-operated individuals in an out-patient setting.

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 August 2021
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: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

- Interview of history of RYGB-surgery, PBH and neuroglycopenia
- Review of inclusion and exclusion criteria
- Blood pressure and pulse measurement
- Weight and height measurement
- ECG recording

Pre-assignment

Screening details:

- 14 days of blinded CGM recording verifying PBH at least three times a week

Period 1

Period 1 title	Overall placebo and 120 ug dasiglucagon (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The outpatient treatment period comprised two consecutive unbroken treatment periods of either four weeks of self-administered placebo or dasiglucagon in random and double-blind order and with a one-week interposed washout period. Placebo and dasiglucagon were contained in indistinguishable cartridges. All participants and study personnel maintained blinding throughout the study.

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Four weeks of self-administered placebo SC injections at the onset of hypoglycemia

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.03 ml of placebo

Arm title	120 ug dasiglucagon

Arm description:

Four weeks of self-administered 120 ug of dasiglucagon at the onset of hypoglycemia

Arm type	Experimental
Investigational medicinal product name	Dasiglucagon
Investigational medicinal product code	
Other name	ZP4207
Pharmaceutical forms	Solution for injection in multidose container
Routes of administration	Subcutaneous use

Dosage and administration details:

120 ug of dasiglucagon (4 mg/ml) using a pen which was a multi-dose reusable pen injector for single-patient use with a replaceable cartridge-based system. The cartridge is pre-filled by the manufacturer (Zealand Pharma) and inserted by the user (participants).

Number of subjects in period 1	Placebo	120 ug dasiglucagon
Started	24	24
Completed	24	24

Baseline characteristics

Reporting groups	
Reporting group title	Overall placebo and 120 ug dasiglucagon
Reporting group description:	
24 subjects at baseline	

Reporting group values	Overall placebo and 120 ug dasiglucagon	Total	
Number of subjects	24	24	
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)	24	24	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	23	23	
Male	1	1	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Four weeks of self-administered placebo SC injections at the onset of hypoglycemia	
Reporting group title	120 ug dasiglucagon
Reporting group description:	
Four weeks of self-administered 120 ug of dasiglucagon at the onset of hypoglycemia	

Primary: The percentage of time spent in hypoglycaemia (IG <3.9 mmol/l) assessed by CGM during the out-patient part of the study

End point title	The percentage of time spent in hypoglycaemia (IG <3.9 mmol/l) assessed by CGM during the out-patient part of the study
End point description:	
End point type	Primary
End point timeframe:	
four weeks of self-administered placebo vs four weeks of self-administered dasiglucagon	

End point values	Placebo	120 ug dasiglucagon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: mmol/l				
arithmetic mean (confidence interval 95%)	3.7 (2.6 to 4.8)	2.4 (1.8 to 3.1)		

Statistical analyses

Statistical analysis title	mixed linear model
Statistical analysis description:	
mixed linear model with treatments and periods as fixed factor and a random subject effect	
Comparison groups	Placebo v 120 ug dasiglucagon
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	Mixed models analysis

Secondary: Percentage of time spent in level 2 hypoglycaemia (IG <3.0 mmol/l) as

assessed by CGM during the outpatient part of the study.	
End point title	Percentage of time spent in level 2 hypoglycaemia (IG <3.0 mmol/l) as assessed by CGM during the outpatient part of the study.

End point description:

End point type	Secondary

End point timeframe:

four weeks of self-administered placebo vs four weeks of self-administered dasiglucagon

End point values	Placebo	120 ug dasiglucagon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: mmol/l				
arithmetic mean (confidence interval 95%)	0.7 (0.5 to 1.0)	0.3 (0.2 to 0.5)		

Statistical analyses

Statistical analysis title	mixed linear model

Statistical analysis description:

mixed linear model with treatments and periods as fixed factor and a random subject effect

Comparison groups	Placebo v 120 ug dasiglucagon
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	Mixed models analysis

Secondary: Frequency of hypoglycaemic events (IG <3.9 mmol/)	
End point title	Frequency of hypoglycaemic events (IG <3.9 mmol/)

End point description:

End point type	Secondary

End point timeframe:

Four weeks of placebo treatment vs four weeks dasiglucagon treatment

End point values	Placebo	120 ug dasiglucagon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Number of events per week				
arithmetic mean (confidence interval 95%)	1.4 (1.0 to 1.7)	1.2 (0.9 to 1.5)		

Statistical analyses

Statistical analysis title	mixed linear model
Statistical analysis description: mixed linear model with treatments and periods as fixed factor and a random subject effect	
Comparison groups	Placebo v 120 ug dasiglucagon
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.16
Method	Mixed models analysis

Secondary: Frequency of level 2 hypoglycaemic events (IG <3.0 mmol/l)

End point title	Frequency of level 2 hypoglycaemic events (IG <3.0 mmol/l)
End point description:	
End point type	Secondary
End point timeframe: Four weeks of placebo treatment vs four weeks dasiglucagon treatment	

End point values	Placebo	120 ug dasiglucagon		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Numbers of events per week				
median (inter-quartile range (Q1-Q3))	0.3 (0.2 to 0.5)	0.2 (0.1 to 0.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: from signed consent form to end of study (0-16 weeks)	
Adverse event reporting additional description: Collected on a weekly basis during phone interviews	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: During the treatment periods, seven participants (29%) treated with dasiglucagon reported a total of 25 incidences of mild-to-moderate nausea compared with two participants (8%) who reported a total of two incidences in the placebo period. These events were primarily driven by three participants who reported 28 adverse events during dasiglucagon treatment, with nausea (20 counts) and dizziness (4 counts) being the most frequent. No adverse events lead to premature discontinuation from the trial

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