Clinical trial results:
Pen-Administered Low-Dose Dasiglucagon for Prevention and Treatment of Hypoglycemia in People with Type 1 Diabetes: A Randomized, Open-Label, Two-Period Crossover Outpatient Study

Summary

EudraCT number	2020-005745-16
Trial protocol	DK
Global end of trial date	28 January 2022

Results information

Result version number	v1 (current)
This version publication date	24 February 2023
First version publication date	24 February 2023

Trial information

Trial identification

Sponsor protocol code	77119

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04764968
WHO universal trial number (UTN)	-
Other trial identifiers	Regional Scientific Ethics Committee: H-21000002

Notes:

Sponsors

Sponsor organisation name	Steno Diabetes Center Copenhagen
Sponsor organisation address	Borgmester Ib Juuls Vej 83, Herlev, Denmark, 2730
Public contact	Christian Laugesen, Steno Diabetes Center Copenhagen, +45 51642387, christian.laugesen@regionh.dk
Scientific contact	Christian Laugesen, Steno Diabetes Center Copenhagen, +45 51642387, christian.laugesen@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	14 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 December 2021
Global end of trial reached?	Yes
Global end of trial date	28 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the efficacy, safety and feasibility of outpatient-utilization of low-dose (80 µg) dasiglucagon administered via an investigational trial device (a multi-dose reusable pen injector) in preventing and treating mild hypoglycemia in insulin pump-treated people type 1 diabetes

Protection of trial subjects:

N/A

Background therapy:

All participants used their regular treatment modality (insulin pump therapy including stand-alone CGM).

Evidence for comparator:

N/A

Actual start date of recruitment	27 April 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)	20
From 65 to 84 years	4

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from the outpatient diabetes clinic at Steno Diabetes Center Copenhagen from May 2021 to November 2021.

Pre-assignment

Screening details:

After providing oral and written informed consent, participants completed a screening visit for assessment of the eligibility criteria. Procedures included routine blood sampling, physical examination, review of medical history and medications as well as registration of baseline characteristics.

Period 1

Period 1 title	Study period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Dasiglucagon period

Arm description:

2-week period where participants managed impending and manifested episodes of hypoglycaemia with pen-administered low-dose (80 µg) s.c. dasiglucagon using a multi-dose reusable pen injector.

Arm type	Experimental
Investigational medicinal product name	dasiglucagon
Investigational medicinal product code	
Other name	CAS15 number: 1544300-84-6, EV Substance code: SUB193123
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administration of s.c. dasiglucagon (80 ug) using a multi-dose reusable pen injector.

Arm title	Usual care period

Arm description:

2-week period where participants managed impending and manifested episodes of hypoglycaemia with usual care (i.e. consumption of carbohydrates)

Arm type	Usual care

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Dasiglucagon period	Usual care period
Started	24	24
Completed	24	24

Baseline characteristics

Reporting groups	
Reporting group title	Study period
Reporting group description:	
All 24 participants included in the study	

Reporting group values	Study period	Total	
Number of subjects	24	24	
Age categorical			
Units: Subjects			
Adults (18-64 years)	20	20	
From 65-84 years	4	4	
Age continuous			
Units: years			
arithmetic mean	47		
standard deviation	± 15	-	
Gender categorical			
Units: Subjects			
Female	14	14	
Male	10	10	
Duration of diabetes			
Units: Years			
arithmetic mean	27		
standard deviation	± 13	-	
Weight			
Units: kilogram(s)			
arithmetic mean	84.2		
standard deviation	± 14.2	-	
Body mass index			
Units: kilogram(s)/square metre			
arithmetic mean	28.3		
standard deviation	± 4.2	-	
Systolic blood pressure			
Units: mmHg			
arithmetic mean	130		
standard deviation	± 15	-	
Diastolic blood pressure			
Units: mmHg			
arithmetic mean	82		
standard deviation	± 7	-	
Hemoglobin A1c			
Units: mmol/mol			
arithmetic mean	56		
standard deviation	± 6	-	
Hemoglobin A1c			
Units: Percentage			
arithmetic mean	7.3		
standard deviation	± 0.5	-	

Duration of insulin pump use Units: Years arithmetic mean standard deviation	 8 ± 1	 -	
Total daily insulin dose Units: Units arithmetic mean standard deviation	 45 ± 20	 -	
Daily basal insulin dose Units: Units arithmetic mean standard deviation	 21 ± 10	 -	
Daily bolus insulin dose Units: Units arithmetic mean standard deviation	 24 ± 11	 -	

Subject analysis sets	
Subject analysis set title	Dasiglucagon period
Subject analysis set type	Full analysis
Subject analysis set description: 2-week period where participants managed impending and manifested episodes of hypoglycaemia with pen-administered low-dose (80 µg) s.c. dasiglucagon using a multi-dose reusable pen injector.	
Subject analysis set title	Usual care period
Subject analysis set type	Full analysis
Subject analysis set description: 2-week period where participants managed impending and manifested episodes of hypoglycaemia with usual care (i.e. consumption of carbohydrates)	

Reporting group values	Dasiglucagon period	Usual care period	
Number of subjects	24	24	
Age categorical Units: Subjects			
Adults (18-64 years) From 65-84 years			
Age continuous Units: years arithmetic mean standard deviation	 ±	 ±	
Gender categorical Units: Subjects			
Female Male			
Duration of diabetes Units: Years arithmetic mean standard deviation	 ±	 ±	
Weight Units: kilogram(s) arithmetic mean standard deviation	 84.2 ± 14.2	 84.2 ± 14.2	

Body mass index Units: kilogram(s)/square metre arithmetic mean standard deviation	 28.3 ± 4.2	 28.3 ± 4.2	
Systolic blood pressure Units: mmHg arithmetic mean standard deviation	 ±	 ±	
Diastolic blood pressure Units: mmHg arithmetic mean standard deviation	 ±	 ±	
Hemoglobin A1c Units: mmol/mol arithmetic mean standard deviation	 ±	 ±	
Hemoglobin A1c Units: Percentage arithmetic mean standard deviation	 7.3 ± 0.5	 7.3 ± 0.5	
Duration of insulin pump use Units: Years arithmetic mean standard deviation	 ±	 ±	
Total daily insulin dose Units: Units arithmetic mean standard deviation	 ±	 ±	
Daily basal insulin dose Units: Units arithmetic mean standard deviation	 ±	 ±	
Daily bolus insulin dose Units: Units arithmetic mean standard deviation	 ±	 ±	

End points

End points reporting groups

Reporting group title	Dasiglucagon period
Reporting group description:	
2-week period where participants managed impending and manifested episodes of hypoglycaemia with pen-administered low-dose (80 µg) s.c. dasiglucagon using a multi-dose reusable pen injector.	
Reporting group title	Usual care period
Reporting group description:	
2-week period where participants managed impending and manifested episodes of hypoglycaemia with usual care (i.e. consumption of carbohydrates)	
Subject analysis set title	Dasiglucagon period
Subject analysis set type	Full analysis
Subject analysis set description:	
2-week period where participants managed impending and manifested episodes of hypoglycaemia with pen-administered low-dose (80 µg) s.c. dasiglucagon using a multi-dose reusable pen injector.	
Subject analysis set title	Usual care period
Subject analysis set type	Full analysis
Subject analysis set description:	
2-week period where participants managed impending and manifested episodes of hypoglycaemia with usual care (i.e. consumption of carbohydrates)	

Primary: Percentage of time in range (3.9-10 mmol/L)

End point title	Percentage of time in range (3.9-10 mmol/L)
End point description:	
End point type	Primary
End point timeframe:	
2-week 'usual care' period and 2-week 'dasiglucagon' period	

End point values	Dasiglucagon period	Usual care period		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: Percentage				
arithmetic mean (standard deviation)	63.5 (± 11)	61.1 (± 15)		

Statistical analyses

Statistical analysis title	Difference between interventions
Statistical analysis description:	
The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect.	
Comparison groups	Dasiglucagon period v Usual care period

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1286
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	5.5

Secondary: Percentage of time below range (<3.9 mmol/L)

End point title	Percentage of time below range (<3.9 mmol/L)

End point description:

End point type	Secondary

End point timeframe:

2-week usual care period and 2-week dasiglucagon period

End point values	Dasiglucagon period	Usual care period		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: Percentage				
arithmetic mean (standard deviation)	2.5 (± 3)	3.1 (± 4)		

Statistical analyses

Statistical analysis title	Difference between intervenstions

Statistical analysis description:

The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect.

Comparison groups	Dasiglucagon period v Usual care period
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1622
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.2

Secondary: Percentage of time above range (>10 mmol/L)

End point title	Percentage of time above range (>10 mmol/L)

End point description:

End point type	Secondary

End point timeframe:

2-week usual care period and 2-week dasiglucagon period

End point values	Dasiglucagon period	Usual care period		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: Percentage				
arithmetic mean (standard deviation)	33.9 (± 13)	35.8 (± 17)		

Statistical analyses

Statistical analysis title	Difference between interventions

Statistical analysis description:

The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect.

Comparison groups	Dasiglucagon period v Usual care period
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.2772
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	1.6

Notes:

[1] - The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect.

Secondary: Coefficient of variation

End point title	Coefficient of variation

End point description:

End point type	Secondary

End point timeframe:

2-week usual care period and 2-week dasiglucagon period

End point values	Dasiglucagon period	Usual care period		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: Percentage				
arithmetic mean (standard deviation)	35.6 (± 4)	35.2 (± 5)		

Statistical analyses

Statistical analysis title	Difference between interventions

Statistical analysis description:

The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect.

Comparison groups	Dasiglucagon period v Usual care period
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.5503
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.8

Notes:

[2] - The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect.

Secondary: Successful cases (%) of hypoglycemia treatment

End point title	Successful cases (%) of hypoglycemia treatment

End point description:

Initial sensor glucose level ≥ 2.2 mmol/l and ≤ 3.9 mmol/l AND sensor glucose level > 3.9 mmol/l 30 minutes post-treatment

End point type	Secondary

End point timeframe:

2-week 'usual care' period and 2-week 'dasiglucagon' period

End point values	Dasiglucagon period	Usual care period		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: Percentage				
number (not applicable)	86	77		

Statistical analyses

Statistical analysis title	Difference between interventions

Statistical analysis description:

The endpoint was evaluated using a logistic regression model with random subject effect using sequence, period, and event baseline sensor glucose value as a covariate.

Comparison groups	Dasiglucagon period v Usual care period
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1597
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	2.86

Secondary: Successful cases (%) of hypoglycemia treatment without subsequent hyperglycemia

End point title	Successful cases (%) of hypoglycemia treatment without subsequent hyperglycemia

End point description:

Initial sensor glucose level ≥ 2.2 mmol/l and ≤ 3.9 mmol/l AND sensor glucose level > 3.9 mmol/l 30 minutes post-treatment AND sensor glucose level ≤ 10 mmol/l during the first two hours post-treatment

End point type	Secondary

End point timeframe:

2-week 'usual care' period and 2-week 'dasiglucagon' period

End point values	Dasiglucagon period	Usual care period		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: Percentage				
number (not applicable)	57	57		

Statistical analyses

Statistical analysis title	Difference between interventions
Statistical analysis description:	
The endpoint was evaluated using a logistic regression model with random subject effect using sequence, period, and event baseline sensor glucose value as a covariate.	
Comparison groups	Dasiglucagon period v Usual care period
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3215
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.27

Secondary: Successful cases (%) of hypoglycemia prevention

End point title	Successful cases (%) of hypoglycemia prevention
End point description:	
Initial sensor glucose level > 3.9 mmol/l AND sensor glucose level < 3.9 for ≤ 15 consecutive minutes during the first two hours post-treatment	
End point type	Secondary
End point timeframe:	
2-week 'usual care' period and 2-week 'dasiglucagon' period	

End point values	Dasiglucagon period	Usual care period		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: Percentage				
number (not applicable)	90	80		

Statistical analyses

Statistical analysis title	Difference between interventions

Statistical analysis description:

The endpoint was evaluated using a logistic regression model with random subject effect using sequence, period, and event baseline sensor glucose value as a covariate.

Comparison groups	Dasiglucagon period v Usual care period
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0177
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	7.41

Secondary: Time (in minutes) from hypoglycemia treatment to euglycemia

End point title	Time (in minutes) from hypoglycemia treatment to euglycemia

End point description:

Minutes from initial sensor glucose level ≥ 2.2 mmol/l and ≤ 3.9 mmol/l to sensor glucose level ≥ 3.9 mmol/l

End point type	Secondary

End point timeframe:

2-week 'usual care' period and 2-week 'dasiglucagon' period

End point values	Dasiglucagon period	Usual care period		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: Minutes				
median (inter-quartile range (Q1-Q3))	16 (12 to 23)	21 (13 to 30)		

Statistical analyses

Statistical analysis title	Difference between interventions

Statistical analysis description:

The endpoint was evaluated using a proportional hazards regression model with gamma-distributed random effect using sequence, period, and event baseline sensor glucose value as a covariate.

Comparison groups	Dasiglucagon period v Usual care period

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0064
Method	Regression, Cox
Parameter estimate	Rate ratio (RR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.11
upper limit	1.87

Secondary: Incidence rate of supplement carbohydrate administration during the first hour following dasiglucagon administration

End point title	Incidence rate of supplement carbohydrate administration during the first hour following dasiglucagon administration

End point description:

End point type	Secondary

End point timeframe:

2-week 'dasiglucagon' period

End point values	Dasiglucagon period			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Number of episodes	22			

Statistical analyses

No statistical analyses for this end point

Secondary: Total daily insulin dose

End point title	Total daily insulin dose

End point description:

End point type	Secondary

End point timeframe:

2-week 'usual care' period and 2-week 'dasiglucagon' period

End point values	Dasiglucagon period	Usual care period		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: Units				
arithmetic mean (standard deviation)	47.1 (± 22)	46.4 (± 20)		

Statistical analyses

Statistical analysis title	Difference between interventions

Statistical analysis description:

The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect.

Comparison groups	Dasiglucagon period v Usual care period
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5148
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	2.9

Secondary: Total daily carbohydrate intake

End point title	Total daily carbohydrate intake

End point description:

End point type	Secondary

End point timeframe:

2-week 'dasiglucagon' period

End point values	Dasiglucagon period	Usual care period		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: grams				
arithmetic mean (standard deviation)	171 (± 59)	191 (± 66)		

Statistical analyses

Statistical analysis title	Difference between interventions

Statistical analysis description:

The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect.

Comparison groups	Dasiglucagon period v Usual care period
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-20
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34
upper limit	-6

Secondary: Patient-reported outcome

End point title	Patient-reported outcome

End point description:

Percentage of participants scoring a favorable outcome on the patient-reported outcome questionnaire ("How likely is it that you, given the option, would use dasiglucagon as part of your diabetes management?" (Answer options: Very unlikely, unlikely, likely, very likely).

End point type	Secondary

End point timeframe:

At the end-of-study visit

End point values	Dasiglucagon period			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Percentage				
number (not applicable)	96			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 2-week 'usual care' period and 2-week 'dasiglucagon' period	
Assessment type	Systematic
Dictionary used	
Dictionary name	N/A
Dictionary version	N/A
Reporting groups	
Reporting group title	Dasiglucagon period
Reporting group description: -	
Reporting group title	Usual care period
Reporting group description: -	

Serious adverse events	Dasiglucagon period	Usual care period	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (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	Dasiglucagon period	Usual care period	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 24 (45.83%)	10 / 24 (41.67%)	
Cardiac disorders			
Palpitations			
subjects affected / exposed	3 / 24 (12.50%)	1 / 24 (4.17%)	
occurrences (all)	4	1	
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 24 (41.67%)	8 / 24 (33.33%)	
occurrences (all)	36	22	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	8 / 24 (33.33%)	4 / 24 (16.67%)	
occurrences (all)	34	17	

Vomiting			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	1	
Stomachache			
subjects affected / exposed	4 / 24 (16.67%)	3 / 24 (12.50%)	
occurrences (all)	16	15	

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