



Clinical trial results:

The HYPO-AVOID STUDY: Low-dose Glucagon and Advanced Hybrid Closed-loop System for Prevention of Exercise-Induced Hypoglycaemia in People with Type 1 Diabetes

Summary

EudraCT number	2021-004993-68
Trial protocol	DK
Global end of trial date	01 November 2024

Results information

Result version number	v1 (current)
This version publication date	09 July 2025
First version publication date	09 July 2025

Trial information

Trial identification

Sponsor protocol code	85256
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Steno Diabetes Center Copenhagen
Sponsor organisation address	Borgmester Ib Juuls Vej 89, Købehavn, Denmark, 2730
Public contact	Sissel Lundemose, Steno Diabetes Center Copenhagen, +45 23742764, sissel.lundemose@regionh.dk
Scientific contact	Sissel Lundemose, Steno Diabetes Center Copenhagen, +45 23742764, sissel.lundemose@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	01 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 October 2024
Global end of trial reached?	Yes
Global end of trial date	01 November 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the effect of low-dose glucagon (single 150 µg dose) administered immediately before aerobic exercise (visit B) versus a control trial without glucagon (visit C) on glucose responses during and after exercise in individuals with AHCL-treated T1D.

Protection of trial subjects:

Visual analog scale 1-100 (VAS) was used to trace adverse events.

Background therapy:

All participants with type 1 diabetes (T1D) were treated with a Minimed Medtronic 780G insulin pump (Automated Insulin Delivery (AID) system)

Evidence for comparator:

We hypothesize that low-dose glucagon administered s.c. before aerobic exercise is superior to no glucagon regarding glucose control around exercise in people with T1D using AID therapy.

The objective was to compare the effect of low-dose glucagon (single 150 µg dose) administered immediately before aerobic exercise versus a control trial without glucagon on glucose responses during and after exercise in individuals with AID-treated T1D.

Actual start date of recruitment	01 January 2022
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	Denmark: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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)	9
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The HYPO-AVOID study will include individuals with AID-treated (Minimed Medtronic 780G) T1D, and the participants will be recruited from the clinic at Steno Diabetes Center Copenhagen.

Pre-assignment

Screening details:

Inclusion criteria

- Age $\geq$ 18 years
- Type 1 diabetes $\geq$ 2 years
- Using the AHCL system MiniMed 780G $\geq$ 4 weeks
- Novorapid use $\geq$ 1 week

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Glucagon (Visit 1)

Arm description:

Immediately before exercise start ($t = 0$), 150 μ g s.c. glucagon will be administrated in the abdominal area

Arm type	Experimental
Investigational medicinal product name	glucagon
Investigational medicinal product code	SUB02347MIG
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Injection

Dosage and administration details:

150 micrograms

Arm title	No glucagon (Visit 2)
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Arm description:

- Immediately before exercise start ($t = 0$), no glucagon will be administrated.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Glucagon (Visit 1)	No glucagon (Visit 2)
Started	10	10
Completed	10	10

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial
Reporting group description: -	

Reporting group values	Overall Trial	Total	
Number of subjects	10	10	
Age categorical			
Units: Subjects			
Adults (18-64 years)	9	9	
From 65-84 years	1	1	
Age continuous			
Units: years			
median	50		
full range (min-max)	42 to 67	-	
Gender categorical			
Units: Subjects			
Female	4	4	
Male	6	6	
BMI			
(kg/m2)			
Units: kg/m2			
median	26		
full range (min-max)	21 to 29	-	
Type 1 duration			
Units: years			
median	22		
full range (min-max)	14 to 44	-	
HbA1c			
Units: mmol/mol			
median	55		
full range (min-max)	47 to 69	-	
Time in Range			
Percentage			
Units: 0-100			
median	77		
full range (min-max)	69 to 79	-	
Time below range			
Percentage			
Units: 0-100			
median	1		
full range (min-max)	1 to 10	-	

End points

End points reporting groups

Reporting group title	Glucagon (Visit 1)
Reporting group description: Immediately before exercise start (t = 0), 150 µg s.c. glucagon will be administrated in the abdominal area	
Reporting group title	No glucagon (Visit 2)
Reporting group description: Immediately before exercise start (t = 0), no glucagon will be administrated.	

Primary: • Difference in percentage of time in target glucose range (PG: 3.9 - 10.0 mmol/l) during and for 1-hour after dynamic physical exercise (0 min to +105min) between visits 1 and 2

End point title	• Difference in percentage of time in target glucose range (PG: 3.9 - 10.0 mmol/l) during and for 1-hour after dynamic physical exercise (0 min to +105min) between visits 1 and 2
End point description:	
End point type	Primary
End point timeframe: From 0-105 min.	

End point values	Glucagon (Visit 1)	No glucagon (Visit 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: %				
median (inter-quartile range (Q1-Q3))	100 (91 to 100)	100 (100 to 100)		

Statistical analyses

Statistical analysis title	Wilcoxon Rank Test
Comparison groups	No glucagon (Visit 2) v Glucagon (Visit 1)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.18
Method	Wilcoxon (Mann-Whitney)

Secondary: • Difference in incidence rate of hypoglycemic events (PG<3.9 mmol/l) (0 min to +105min) between visits 1 and 2

End point title	• Difference in incidence rate of hypoglycemic events (PG<3.9 mmol/l) (0 min to +105min) between visits 1 and 2
End point description:	
End point type	Secondary
End point timeframe:	
From 0 to 105 min	

End point values	Glucagon (Visit 1)	No glucagon (Visit 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Number				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: • Difference in percentage of time below target glucose range (PG<3.9 mmol/l) (0 min to +105min) between visits 1 and 2

End point title	• Difference in percentage of time below target glucose range (PG<3.9 mmol/l) (0 min to +105min) between visits 1 and 2
End point description:	
End point type	Secondary
End point timeframe:	
From 0 to 105 min	

End point values	Glucagon (Visit 1)	No glucagon (Visit 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: %				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

Statistical analysis title	Wilcoxon Rank Test
Comparison groups	Glucagon (Visit 1) v No glucagon (Visit 2)

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Secondary: • Difference in percentage of time above target glucose range (PG>10.0 mmol/l) (0 min to +105min) between visits 1 and 2

End point title	• Difference in percentage of time above target glucose range (PG>10.0 mmol/l) (0 min to +105min) between visits 1 and 2
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End point description:

End point type	Secondary
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End point timeframe:

From 0 to 105 min

End point values	Glucagon (Visit 1)	No glucagon (Visit 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: %				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

Statistical analysis title	Wilcoxon Rank Test
Comparison groups	Glucagon (Visit 1) v No glucagon (Visit 2)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	Wilcoxon (Mann-Whitney)

Secondary: • Difference in nadir PG concentration (0 min to +105min) between visits 1 and 2

End point title	• Difference in nadir PG concentration (0 min to +105min) between visits 1 and 2
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End point description:

End point type	Secondary
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End point timeframe:

From 0 to 105 min

End point values	Glucagon (Visit 1)	No glucagon (Visit 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: mmol/l				
median (inter-quartile range (Q1-Q3))	5.8 (5.2 to 6.9)	5.8 (4.9 to 6.5)		

Statistical analyses

Statistical analysis title	Wilcoxon Rank Test
Comparison groups	Glucagon (Visit 1) v No glucagon (Visit 2)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.41
Method	Wilcoxon (Mann-Whitney)

Secondary: • Difference in peak PG concentration (0 min to +105min) between visits 1 and 2

End point title	• Difference in peak PG concentration (0 min to +105min) between visits 1 and 2
End point description:	
End point type	Secondary
End point timeframe:	
From 0 to 105 min	

End point values	Glucagon (Visit 1)	No glucagon (Visit 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: mmol/l				
arithmetic mean (standard error)	9.3 ($\pm$ 1.8)	7.4 ($\pm$ 1.4)		

Statistical analyses

Statistical analysis title	TTEST
Comparison groups	Glucagon (Visit 1) v No glucagon (Visit 2)

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	t-test, 2-sided

Secondary: • Difference in mean PG concentration (0 min to +105min) between visits 1 and 2

End point title	• Difference in mean PG concentration (0 min to +105min) between visits 1 and 2
End point description:	
End point type	Secondary
End point timeframe:	
From min0 to 105 min	

End point values	Glucagon (Visit 1)	No glucagon (Visit 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: mmol/l				
median (standard deviation)	8.3 (± 1.8)	6.7 (± 1.3)		

Statistical analyses

Statistical analysis title	TTEST
Comparison groups	Glucagon (Visit 1) v No glucagon (Visit 2)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	t-test, 2-sided

Secondary: • Difference in PG Area Under the Curve (AUC) (0 min to +105min) between visits 1 and 2

End point title	• Difference in PG Area Under the Curve (AUC) (0 min to +105min) between visits 1 and 2
End point description:	
End point type	Secondary
End point timeframe:	
From min 0 to min 105.	

End point values	Glucagon (Visit 1)	No glucagon (Visit 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: mmol/l*min				
log mean (inter-quartile range (Q1-Q3))	824.2 (782.3 to 941.2)	686.2 (612.2 to 821.1)		

Statistical analyses

Statistical analysis title	log TTEST
Comparison groups	Glucagon (Visit 1) v No glucagon (Visit 2)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	t-test, 2-sided

Secondary: • Difference in standard deviation in PG concentrations (0 min to +105min) between visits 1 and 2

End point title	• Difference in standard deviation in PG concentrations (0 min to +105min) between visits 1 and 2
End point description:	
End point type	Secondary
End point timeframe:	
From min 0 to min 150	

End point values	Glucagon (Visit 1)	No glucagon (Visit 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: mmol/l				
median (inter-quartile range (Q1-Q3))	1.0 (0.7 to 1.2)	0.5 (0.3 to 0.5)		

Statistical analyses

Statistical analysis title	Wilcoxon Rank Test
Comparison groups	Glucagon (Visit 1) v No glucagon (Visit 2)

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Wilcoxon (Mann-Whitney)

Secondary: • Difference in coefficient of variation in PG concentrations (0 min to +105min) between visits 1 and 2

End point title	• Difference in coefficient of variation in PG concentrations (0 min to +105min) between visits 1 and 2
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End point description:

End point type	Secondary
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End point timeframe:

From min 0 to min 105.

End point values	Glucagon (Visit 1)	No glucagon (Visit 2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: mmol/l				
median (standard error)	12.3 (± 4.3)	7.3 (± 2.5)		

Statistical analyses

Statistical analysis title	TTEST
Comparison groups	Glucagon (Visit 1) v No glucagon (Visit 2)
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.01
Method	t-test, 2-sided

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

From min 0 to min 105

Adverse event reporting additional description:

Adverse events (nausea, stomach-ache, injections site pain, headache, and palpitation) were assessed using a 0-100 visual analogue score (VAS) before (baseline), after exercise, and at the end of the trial to evaluate the occurrence of any adverse events.

Assessment type	Systematic
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Dictionary used

Dictionary name	VAS
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Dictionary version	1
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Reporting groups

Reporting group title	Entire trial
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Reporting group description:

For the entire trial. No adverse events were reported.

Serious adverse events	Entire trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Entire trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		

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: No adverse events were recorded during 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