



## Clinical trial results: The impact of subcutaneous glucagon before, during and after exercise. A study in patients with type 1 diabetes mellitus

### Summary

EudraCT number	2016-002127-28
Trial protocol	DK
Global end of trial date	07 July 2017

### Results information

Result version number	v1 (current)
This version publication date	22 December 2019
First version publication date	22 December 2019

### Trial information

#### Trial identification

Sponsor protocol code	16016762
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#### Additional study identifiers

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

Notes:

### Sponsors

Sponsor organisation name	Hvidovre Univeraity Hospital
Sponsor organisation address	Kettegård Allé 30, Hvidovre, Denmark, 2650
Public contact	Isabelle, Hvidovre University Hospital, +45 51519085, Isabelle.Isa.Kristin.Steineck@regionh.dk
Scientific contact	Isabelle, Hvidovre University Hospital, +45 51519085, Isabelle.Isa.Kristin.Steineck@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	Interim
Date of interim/final analysis	29 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 July 2017
Global end of trial reached?	Yes
Global end of trial date	07 July 2017
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

1. To compare the increase in plasma glucose after 200µg glucagon given either after exercise or after resting for 45 minutes.

Protection of trial subjects:

1. Visual analogue score to collect data on nausea, pain, sweating and heartbeats
2. If a subject would have had a low blood glucose under 2.5 mmol/l then we would have stopped the trial

Background therapy:

Continuous subcutaneous insulin pump therapy

Evidence for comparator: -

Actual start date of recruitment	04 July 2016
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: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	13
From 65 to 84 years	1



## Subject disposition

### Recruitment

Recruitment details:

Participants were recruited from the outpatient diabetes clinic at Copenhagen University Hospital in Hvidovre in the period September 2016 to May 2017.

### Pre-assignment

Screening details:

The screening was performed after an overnight fast. Information was collected on sex, age, race, diabetes duration, allergies, medical history and medications; height, weight, blood pressure and heart rate were measured; questionnaires to identify hypoglycemia unawareness were filled out and a 12-lead electrocardiography.

### Pre-assignment period milestones

Number of subjects started	18 <sup>[1]</sup>
Number of subjects completed	14

### Pre-assignment subject non-completion reasons

Reason: Number of subjects	Pregnancy: 1
Reason: Number of subjects	Lack of time: 3

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: I included 18 but only 14 completed

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

### Arms

Are arms mutually exclusive?	No
<b>Arm title</b>	Glucagon after Cycling

Arm description:

Participants consumed a standardized breakfast two hours prior to 45 minutes of cycling. A subcutaneous injection of 200 µg glucagon was given after cycling and frequent blood sampling occurred until two hours after exercise.

Arm type	Active comparator
Investigational medicinal product name	GlucaGen
Investigational medicinal product code	SUB02347MIG
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

200 micro gram given subcutaneously in abdominal wall given one time after 45 minutes of cycling

<b>Arm title</b>	Glucagon after Resting
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Arm description:

Participants consumed a standardized breakfast two hours prior to 45 minutes of resting. A subcutaneous injection of 200 µg glucagon was given after resting and frequent blood sampling occurred until two hours after the injection of glucagon.

Arm type	control
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Investigational medicinal product name	GlucaGen
Investigational medicinal product code	SUB02347MIG
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 200 micro gram given subcutaneously in abdominal wall given one time after 45 minutes of resting	
<b>Arm title</b>	Glucagon before cycling

Arm description:

Participants consumed a standardized breakfast two hours prior to 45 minutes of cycling. A subcutaneous injection of 200 µg glucagon was given before cycling and frequent blood sampling occurred until two hours after exercise.

Arm type	Active comparator
Investigational medicinal product name	GlucaGen
Investigational medicinal product code	SUB02347MIG
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

200 micro gram given subcutaneously in abdominal wall given one time before 45 minutes of cycling

<b>Number of subjects in period 1</b>	Glucagon after Cycling	Glucagon after Resting	Glucagon before cycling
Started	14	14	13
Completed	14	14	13

## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
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Reporting group description:

Fourteen insulin pump-treated individuals with type 1 diabetes completed three visits in a randomized, placebo-controlled, single-blinded crossover study. Baseline (mean and range) HbA1c 54 (43-65) mmol/mol or 7.1 (6.1-8.1) %, age 45 (23-66) years, BMI 26 (21-30) kg/m<sup>2</sup>, diabetes duration 26 (8-51) years.

Reporting group values	Overall trial	Total	
Number of subjects	14	14	
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)	13	13	
From 65-84 years	1	1	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	45		
full range (min-max)	23 to 66	-	
Gender categorical			
Units: Subjects			
Female	6	6	
Male	8	8	

### Subject analysis sets

Subject analysis set title	Primary endpoint
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Subject analysis set type	Full analysis
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Subject analysis set description:

The subjects in the study

Reporting group values	Primary endpoint		
Number of subjects	14		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	13		
From 65-84 years	1		
85 years and over	0		
Age continuous Units: years arithmetic mean full range (min-max)			
Gender categorical Units: Subjects			
Female			
Male			

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## End points

### End points reporting groups

Reporting group title	Glucagon after Cycling
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Reporting group description:

Participants consumed a standardized breakfast two hours prior to 45 minutes of cycling. A subcutaneous injection of 200 µg glucagon was given after cycling and frequent blood sampling occurred until two hours after exercise.

Reporting group title	Glucagon after Resting
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Reporting group description:

Participants consumed a standardized breakfast two hours prior to 45 minutes of resting. A subcutaneous injection of 200 µg glucagon was given after resting and frequent blood sampling occurred until two hours after the injection of glucagon.

Reporting group title	Glucagon before cycling
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Reporting group description:

Participants consumed a standardized breakfast two hours prior to 45 minutes of cycling. A subcutaneous injection of 200 µg glucagon was given before cycling and frequent blood sampling occurred until two hours after exercise.

Subject analysis set title	Primary endpoint
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Subject analysis set type	Full analysis
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Subject analysis set description:

The subjects in the study

### Primary: The glucose response to glucagon when glucagon was given after cycling compared with after resting

End point title	The glucose response to glucagon when glucagon was given after cycling compared with after resting <sup>[1]</sup>
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End point description:

End point type	Primary
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End point timeframe:

120 minutes after the injection of glucagon

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Not applicable -please see article for further details

End point values	Glucagon after Cycling	Glucagon after Resting		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: mmol/l				
number (not applicable)	2.6	1.8		

### Statistical analyses

Statistical analysis title	Primary outcome
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Statistical analysis description:

A paired t-test was used to compare the logarithmic incremental peak plasma glucose after cycling with after resting.

Comparison groups	Glucagon after Cycling v Glucagon after Resting
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Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other <sup>[2]</sup>
P-value	= 0.02
Method	t-test, 2-sided

Notes:

[2] - Obs: This was a crossover study so the number of subjects was not 28 but 14 because it was the same subjects who did the 2 arms.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

120 minutes after the glucagon injection

Adverse event reporting additional description:

Visual analogue scale given after the glucagon injection that was done in clinic

Assessment type	Systematic
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### Dictionary used

Dictionary name	Visual analogue scal
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Dictionary version	na
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### Reporting groups

Reporting group title	Glucagon after Cycling
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Reporting group description:

Participants consumed a standardized breakfast two hours prior to 45 minutes of cycling. A subcutaneous injection of 200 µg glucagon was given after cycling and frequent blood sampling occurred until two hours after exercise.

Reporting group title	Glucagon after Resting
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Reporting group description:

Participants consumed a standardized breakfast two hours prior to 45 minutes of resting. A subcutaneous injection of 200 µg glucagon was given after resting and frequent blood sampling occurred until two hours after the injection of glucagon.

Reporting group title	Glucagon before cycling
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Reporting group description:

Participants consumed a standardized breakfast two hours prior to 45 minutes of cycling. A subcutaneous injection of 200 µg glucagon was given before cycling and frequent blood sampling occurred until two hours after exercise.

<b>Serious adverse events</b>	Glucagon after Cycling	Glucagon after Resting	Glucagon before cycling
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	0 / 14 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

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

<b>Non-serious adverse events</b>	Glucagon after Cycling	Glucagon after Resting	Glucagon before cycling
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	1 / 14 (7.14%)
Gastrointestinal disorders			
Nausea	Additional description: One participant consistently reported nausea (mean VAS increased 2.83 cm) after glucagon injection in all three study visits.		

subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	1 / 14 (7.14%)
occurrences (all)	1	1	1

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 November 2016	1. We included subjects with age up to 70 years old instead of age up to 65 years old. 2. In the first version of the protocol we included participants with " Sedentary or mild physical activity: Less than 150 minutes of moderate-intensity aerobic physical activity throughout the week and less than 75 minutes of vigorous-intensity aerobic physical activity throughout the week ." We deleted this inclusion criteria this 3. We added a new exclusion criteria: We added: "People with vigorous intensity aerobic physical activity such as swimming, jogging, aerobics, football, tennis, gym, workout etc, more than 3 hours or more per week. "

Notes:

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### 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.

Not applicable. See article for details.

Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30643924>