Clinical trial results:
Dual-Hormone Closed-Loop Glucose Control in Adolescents with Type 1 Diabetes

Summary

EudraCT number	2020-005836-31
Trial protocol	DK
Global end of trial date	26 April 2022

Results information

Result version number	v1 (current)
This version publication date	11 September 2022
First version publication date	11 September 2022

Trial information

Trial identification

Sponsor protocol code	DHCL2021

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04949867
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Steno Diabetes Center Copenhagen
Sponsor organisation address	Borgmester Ib Juuls Vej 83, Herlev, Denmark, 2730
Public contact	Ajenthen G Ranjan, Steno Diabetes Center Copenhagen, 45 23742766, Ajenthen.Ranjan@regionh.dk
Scientific contact	Ajenthen G Ranjan, Steno Diabetes Center Copenhagen, 45 23742766, Ajenthen.Ranjan@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	16 June 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 April 2022
Global end of trial reached?	Yes
Global end of trial date	26 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aims of this two-phase project are to 1) demonstrate proof-of-concept and 2) to compare dual-hormone with single-hormone closed-loop glucose control.

Protection of trial subjects:

Participants were offered numbing creme before canulation for plasma sampling.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 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: 11
Worldwide total number of subjects	11
EEA total number of subjects	11

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)	10
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from the outpatient clinic at Herlev Pediatric Department and Steno Diabetes Center Copenhagen from September 2021 to March 2022

Pre-assignment

Screening details:

Parents of participants provided written informed consent, participants ages 15 years and up provided written informed assent. Afterwards they completed a screening visit for assessment of eligibility criteria. Procedures included physical examination, review of medical records and medications as well as routine blood sampling.

Period 1

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

Blinding implementation details:

Participants were blinded to the study medication

Arms

Are arms mutually exclusive?	No
Arm title	Dual-Hormone Closed-Loop

Arm description:

Pump 1: Fiasp, Pump 2: Glucagon

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

Dosage and administration details:

Particpants were fitted with Glucagon pump at t=0, which was inserted subcutanously. Doses were calculated by the algorithm used in the study, DiaCon APS.

Investigational medicinal product name	FiAsp
Investigational medicinal product code	SUB08195MIG
Other name	
Pharmaceutical forms	Solution for solution for injection, Solution for solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Particpants were fitted with insulin pump at time T=0, which was inserted subcutanuosly. Dosages were calculated by the algorithm used in the study, DiaCon APS.

Arm title	Single-Hormone Closed-Loop

Arm description:

Pump 1: FiAsp
Pump 2: Saline (not set for injection)

Arm type	Active comparator

Investigational medicinal product name	FiAsp
Investigational medicinal product code	SUB08195MIG
Other name	
Pharmaceutical forms	Solution for solution for infusion, Solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Particpants were fitted with insulin pump at time T=0, which was inserted subcutanuosly. Dosages were calculated by the algorithm used in the study, DiaCon APS.

Number of subjects in period 1	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop
Started	11	11
Completed	11	11

Baseline characteristics

Reporting groups	
Reporting group title	Study period (overall period)

Reporting group description: -

Reporting group values	Study period (overall period)	Total	
Number of subjects	11	11	
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)	10	10	
Adults (18-64 years)	1	1	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	14.8		
standard deviation	± 1.47	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	9	9	
BMI Units: kg/m^2			
arithmetic mean	21.4		
standard deviation	± 2.42	-	
Diabetes Duration Units: Years			
arithmetic mean	5.73		
standard deviation	± 2.45	-	
Total Daily Insulin Units: U/kg			
arithmetic mean	0.942		
standard deviation	± 0.256	-	
Time in range (3.9 - 10.0 mmol/L) Units: Percentage			
median	54		
inter-quartile range (Q1-Q3)	46 to 73	-	
Time below range (<3.9 mmol/L) Units: Percentage			
median	3		
inter-quartile range (Q1-Q3)	1.5 to 6.5	-	

Time above range (>10.0 mmol/L) Units: Percentage			
median	43		
inter-quartile range (Q1-Q3)	22.5 to 52	-	
HbA1c Units: millimole(s)/litre			
arithmetic mean	54.6		
standard deviation	± 9.2	-	

End points

End points reporting groups

Reporting group title	Dual-Hormone Closed-Loop
Reporting group description: Pump 1: Fiasp, Pump 2: Glucagon	
Reporting group title	Single-Hormone Closed-Loop
Reporting group description: Pump 1: FiAsp Pump 2: Saline (not set for injection)	

Primary: Percentage of time with glucose values < 3.9 mmol/l as measured by CGM

End point title	Percentage of time with glucose values < 3.9 mmol/l as measured by CGM[1]
End point description:	
End point type	Primary
End point timeframe: Evaluation is performed after completion of the second study visit, i.e., after two times 26-hours	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Categorical variables were reported as frequencies (percentage), whereas continuous were reported as mean (SD) or median (interquartile range [IQR]). Continuous data was assessed for normality using Shapiro-Wilk test. For normally distributed variables, paired student's t-test were used to conduct pair-wise comparisons between the two groups. For skewedly distributed variables despite log-transformation, the non-parametric Wilcoxon signed-rank test was used. Missing glucose data were esti-mated

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Percentage				
median (inter-quartile range (Q1-Q3))	1.6 (0 to 3.99)	1.28 (0 to 3.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of time with glucose values in the range 3.9-10.0 mmol/l measured by CGM

End point title	Percentage of time with glucose values in the range 3.9-10.0 mmol/l measured by CGM
End point description:	
End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Percentage				
median (inter-quartile range (Q1-Q3))	68.1 (48.7 to 75.4)	75.7 (69.8 to 87.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of carbohydrate interventions to treat hypoglycemia

End point title	Number of carbohydrate interventions to treat hypoglycemia

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Grams				
arithmetic mean (standard deviation)	6.8 (± 12.3)	9.5 (± 15.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of time with glucose values < 3.9 mmol/l as measured by YSI

End point title	Percentage of time with glucose values < 3.9 mmol/l as measured by YSI

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Percentage				
median (inter-quartile range (Q1-Q3))	0.958 (0 to 3.83)	2.56 (0.479 to 8.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of time with glucose values in the range 3.9-10.0 mmol/l measured by YSI

End point title	Percentage of time with glucose values in the range 3.9-10.0 mmol/l measured by YSI

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	66.8 (56.9 to 78.9)	79.6 (75.2 to 87.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of time with glucose values >10.0 mmol/l as measured by CGM

End point title	Percentage of time with glucose values >10.0 mmol/l as

	measured by CGM

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	28.1 (18.4 to 50.0)	23.3 (12.3 to 27.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of time with glucose values >10.0 mmol/l as measured by YSI

End point title	Percentage of time with glucose values >10.0 mmol/l as measured by YSI

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	33.2 (16.1 to 40.7)	11.5 (3.83 to 23.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of time with glucose values < 3.0 mmol/l as measured by CGM

End point title	Percentage of time with glucose values < 3.0 mmol/l as measured by CGM

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	0 (0 to 1.28)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of time with glucose values < 3.0 mmol/l as measured by YSI

End point title	Percentage of time with glucose values < 3.0 mmol/l as measured by YSI

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	0 (0 to 0.16)	0 (0 to 0.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean blood glucose value measured by CGM

End point title	Mean blood glucose value measured by CGM

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: mmol/l				
arithmetic mean (standard deviation)	8.7 (± 3.0)	8.1 (± 3.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean blood glucose value measured by YSI

End point title	Mean blood glucose value measured by YSI

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: mmol/L				
arithmetic mean (standard deviation)	8.43 (± 2.83)	7.51 (± 2.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of hypoglycemic episodes <3.9 mmol/L on CGM

End point title	Number of hypoglycemic episodes <3.9 mmol/L on CGM

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: number	14	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of hypoglycemic episodes <3.9 mmol/L on YSI

End point title	Number of hypoglycemic episodes <3.9 mmol/L on YSI

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Number	11	17		

Statistical analyses

No statistical analyses for this end point

Secondary: CGM glycemic variability as SD

End point title	CGM glycemic variability as SD

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: mmol/L				
arithmetic mean (standard deviation)	8.7 (± 3.0)	8.1 (± 3.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: CGM glycemic variability as CV

End point title	CGM glycemic variability as CV

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
arithmetic mean (standard deviation)	34.7 (± 6.9)	37.3 (± 8.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total insulin dose

End point title	Total insulin dose

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: unit(s)				
arithmetic mean (standard deviation)	57.4 (± 20.1)	57.0 (± 16.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total glucagon dose

End point title	Total glucagon dose[2]

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

Notes:

[2] - 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: Gluacgon was only provided in the one arm. Therefore no reporting in the other arm.

End point values	Dual-Hormone Closed-Loop			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: unit(s)				
median (inter-quartile range (Q1-Q3))	548 (229.1 to 1348.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of manual insulin boluses

End point title	Number of manual insulin boluses

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Number	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of adverse events for nasuea

End point title	Number of adverse events for nasuea

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percentage	27	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of adverse events for headache

End point title	Number of adverse events for headache

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percentage	36	36		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of adverse events for stomach ache

End point title	Number of adverse events for stomach ache

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Percentage	18	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of vomits

End point title	Number of vomits

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: Number	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Difference between actual and participant-estimated-CHO content in meals

End point title	Difference between actual and participant-estimated-CHO content in meals

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
arithmetic mean (standard deviation)	84.4 (± 12.6)	82.8 (± 13.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Composite outcome: Percentage of participants achieving (1) time in range (3.9-10) > 70 %, (2) time in alert hypoglycemia (<3.9 mmol/l) < 4 %, and (3) time in clinical hypoglycemia (<3.0 mmol) < 1% as measured by CGM

End point title	Composite outcome: Percentage of participants achieving (1) time in range (3.9-10) > 70 %, (2) time in alert hypoglycemia (<3.9 mmol/l) < 4 %, and (3) time in clinical hypoglycemia (<3.0 mmol) < 1% as measured by CGM

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
number (not applicable)	27	72		

Statistical analyses

No statistical analyses for this end point

Secondary: Composite outcome: Percentage of participants achieving (1) time in range (3.9-10) > 70 %, (2) time in alert hypoglycemia (<3.9 mmol/l) < 4 %, and (3) time in clinical hypoglycemia (<3.0 mmol) < 1% as measured by YSI

End point title	Composite outcome: Percentage of participants achieving (1) time in range (3.9-10) > 70 %, (2) time in alert hypoglycemia (<3.9 mmol/l) < 4 %, and (3) time in clinical hypoglycemia (<3.0 mmol) < 1% as measured by YSI

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
number (not applicable)	27	36		

Statistical analyses

No statistical analyses for this end point

Secondary: Physical activity intensity measured by ActiGraph GT9X Link

End point title	Physical activity intensity measured by ActiGraph GT9X Link

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
arithmetic mean (standard deviation)	2.8 (± 4.5)	1.5 (± 3.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Sleep efficiency measured by ActiGraph GT9X Link

End point title	Sleep efficiency measured by ActiGraph GT9X Link

End point description:

End point type	Secondary

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
arithmetic mean (standard deviation)	78.5 (± 9.2)	74.0 (± 10.5)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Percentage of time with glucose values < 3.9 mmol/l as measured by CGM during sleep

End point title	Percentage of time with glucose values < 3.9 mmol/l as measured by CGM during sleep

End point description:

End point type	Post-hoc

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 3.48)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Percentage of time with glucose values < 3.9 mmol/l as measured by YSI during sleep

End point title	Percentage of time with glucose values < 3.9 mmol/l as measured by YSI during sleep

End point description:

End point type	Post-hoc

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 5.22)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Percentage of time with glucose values >10.0 mmol/l as measured by CGM during sleep

End point title	Percentage of time with glucose values >10.0 mmol/l as measured by CGM during sleep

End point description:

End point type	Post-hoc

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	30.4 (13.5 to 43.9)	0 (0 to 10)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Percentage of time with glucose values >10.0 mmol/l as measured by YSI

during sleep	
End point title	Percentage of time with glucose values >10.0 mmol/l as measured by YSI during sleep

End point description:

End point type	Post-hoc

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	32.2 (5.22 to 37.8)	0 (0 to 5.22)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Percentage of time with glucose values in range 3.9-10.0 mmol/L as measured by CGM during sleep

End point title	Percentage of time with glucose values in range 3.9-10.0 mmol/L as measured by CGM during sleep

End point description:

End point type	Post-hoc

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	69.6 (52.6 to 86.5)	96.5 (84.3 to 100)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: percentage of time with glucose values in range 3.9-10.0 mmol/l as measured by YSI during sleep

End point title	percentage of time with glucose values in range 3.9-10.0 mmol/l as measured by YSI during sleep

End point description:

End point type	Post-hoc

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	67.8 (60.4 to 89.6)	89.6 (82.6 to 100)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Percentage of time with glucose values < 3.9 mmo/l as measured by CGM during and after exercise

End point title	Percentage of time with glucose values < 3.9 mmo/l as measured by CGM during and after exercise

End point description:

End point type	Post-hoc

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Percentage of time with glucose values < 3.9 mmol/l as measured by YSI during and after exercise

End point title	Percentage of time with glucose values < 3.9 mmol/l as measured by YSI during and after exercise

End point description:

End point type	Post-hoc

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	0 (0 to 4.84)	0 (0 to 14.5)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: percentage of time with glucose values in range 3.9-10.0 mmol/L as measured by CGM during and after exericse

End point title	percentage of time with glucose values in range 3.9-10.0 mmol/L as measured by CGM during and after exericse

End point description:

End point type	Post-hoc

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	64.5 (50 to 88.7)	83.9 (80.6 to 100)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Percentage of time with glucose values 3.9-10.0 mmol/l as measured by YSI during and after exercise

End point title	Percentage of time with glucose values 3.9-10.0 mmol/l as measured by YSI during and after exercise

End point description:

End point type	Post-hoc

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	67.7 (32.3 to 99.4)	93.5 (82.3 to 100)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Percentage of time with glucose values >10.0 mmol/l as measured by CGM during and after exercise

End point title	Percentage of time with glucose values >10.0 mmol/l as measured by CGM during and after exercise

End point description:

End point type	Post-hoc

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: perc				
median (inter-quartile range (Q1-Q3))	22.6 (0 to 37.1)	12.9 (0 to 19.4)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Percentage of time with glucose values >10.0 mmol/l as measured by YSI during and after exercise

End point title	Percentage of time with glucose values >10.0 mmol/l as measured by YSI during and after exercise

End point description:

End point type	Post-hoc

End point timeframe:

Evaluation is performed after completion of the second study session, i.e. after two times 26-hours

End point values	Dual-Hormone Closed-Loop	Single-Hormone Closed-Loop		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	11		
Units: percent				
median (inter-quartile range (Q1-Q3))	1.18 (0 to 58.1)	0 (0 to 3.23)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Evaluation of adverse events were performed during study sessions, i.e., two times 26 hours per participant

Adverse event reporting additional description:

Adverse effects (nausea, headache, stomachache, palpitations, vomit, hunger and sweat) were scored using a 0-100 visual analog scale (VAS) seven times during each study session (at the start, before dinner, breakfeast, lunch, snack and exercise session as well as at the end) to evaluate whether adverse events had occured during the intervention.

Assessment type	Systematic

Dictionary used

Dictionary name	None
Dictionary version	0

Reporting groups

Reporting group title	Dual-Hormone Closed-loop (DH)

Reporting group description:

Study session with insulin-glucagon in the system

Reporting group title	Single-Hormone Closed-loop (SH)

Reporting group description:

Study session with insulin-saline in pumps

Serious adverse events	Dual-Hormone Closed-loop (DH)	Single-Hormone Closed-loop (SH)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (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	Dual-Hormone Closed-loop (DH)	Single-Hormone Closed-loop (SH)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 11 (36.36%)	4 / 11 (36.36%)	
General disorders and administration site conditions			
Nausea			
subjects affected / exposed	3 / 11 (27.27%)	0 / 11 (0.00%)	
occurrences (all)	3	0	
Headache			

subjects affected / exposed	4 / 11 (36.36%)	4 / 11 (36.36%)	
occurrences (all)	4	4	
Stomachache			
subjects affected / exposed	1 / 11 (9.09%)	2 / 11 (18.18%)	
occurrences (all)	1	2	

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