



Clinical trial results:

A randomized, double-blind trial of single doses of ZP4207 administered s.c. to hypoglycemic Type 1 diabetic patients to describe the pharmacokinetics and pharmacodynamics of ZP4207 as compared to marketed glucagon

Summary

EudraCT number	2015-005287-41
Trial protocol	DE
Global end of trial date	03 June 2016

Results information

Result version number	v1 (current)
This version publication date	18 November 2020
First version publication date	18 November 2020

Trial information

Trial identification

Sponsor protocol code	ZP4207-15126
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02660008
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Zealand Pharma A/S
Sponsor organisation address	Sydmarken 11, Søborg, Denmark, 2860
Public contact	Lena Skærbye List, Zealand Pharma A/S, +45 5060 3842, llist@zealandpharma.com
Scientific contact	Ramin Tehranchi, Zealand Pharma A/S, +45 5060 3793, rtehranchi@zealandpharma.com

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	06 January 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 June 2016
Global end of trial reached?	Yes
Global end of trial date	03 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the pharmacokinetic (PK) and pharmacodynamic (PD) properties of ZP4207 in the final formulation following a single s.c. dose administered to hypoglycaemic Type 1 diabetic (T1D) patients

Protection of trial subjects:

The trial was conducted in accordance of the World Medical Association Declaration of Helsinki, current guidelines for GCP and local regulations

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 January 2016
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	Germany: 58
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	58
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients were recruited from a single centre in Germany.

Pre-assignment

Screening details:

76 patients were screened and 58 patients were eligible and randomized.

Period 1

Period 1 title	Overall trial period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	No
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Arm title	Group 1 0.1 mg dasiglucagon
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Arm description:

Group 1 parallel design 0.1 mg dasiglucagon or 1.0 mg GlucaGen

Arm type	Experimental
Investigational medicinal product name	Dasiglucagon
Investigational medicinal product code	ZP4207
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

0.1 mg administered as a single dose

Arm title	Group 2 0.3 mg dasiglucagon
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Arm description:

Group 2 crossover design 0.3 mg dasiglucagon with 0.5 mg GlucaGen

Arm type	Experimental
Investigational medicinal product name	Dasiglucagon
Investigational medicinal product code	ZP4207
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

0.3 mg administered as a single dose

Arm title	Group 3 0.6 mg dasiglucagon
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Arm description:

Group 3 crossover design 0.6 mg dasiglucagon with 1.0 mg GlucaGen

Arm type	Experimental
Investigational medicinal product name	Dasiglucagon
Investigational medicinal product code	ZP4207
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:
0.6 mg administered as a single dose

Arm title	Group 4 1.0 mg dasiglucagon
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Arm description:

Group 4 crossover design 1.0 mg dasiglucagon with 1.0 mg GlucaGen

Arm type	Experimental
Investigational medicinal product name	Dasiglucagon
Investigational medicinal product code	ZP4207
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1.0 mg administered as a single dose

Arm title	Group 2 0.5 mg GlucaGen
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Arm description:

Group 2 crossover design 0.3 mg dasiglucagon with 0.5 mg GlucaGen

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

Dosage and administration details:

0.5 mg administered as a single dose

Arm title	Group 3 1.0 mg GlucaGen
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Arm description:

Group 3 crossover design 0.6 mg dasiglucagon with 1.0 mg GlucaGen

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

Dosage and administration details:

1.0 mg administered as a single dose

Arm title	Group 1 1.0 mg GlucaGen
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Arm description:

Group 1 parallel design 0.1 mg dasiglucagon or 1.0 mg GlucaGen

Arm type	Active comparator
Investigational medicinal product name	GlucaGen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1.0 mg administered as a single dose

Arm title	Group 4 1.0 mg GlucaGen
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Arm description:

Group 4 crossover design 1.0 mg dasiglucagon with 1.0 mg GlucaGen

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

Dosage and administration details:

1.0 mg administered as a single dose

Number of subjects in period 1	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon
Started	6	17	17
Completed	6	16	17
Not completed	0	1	0
Consent withdrawn by subject	-	1	-

Number of subjects in period 1	Group 4 1.0 mg dasiglucagon	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen
Started	16	17	17
Completed	16	17	16
Not completed	0	0	1
Consent withdrawn by subject	-	-	1

Number of subjects in period 1	Group 1 1.0 mg GlucaGen	Group 4 1.0 mg GlucaGen
Started	2	16
Completed	2	16
Not completed	0	0
Consent withdrawn by subject	-	-

Baseline characteristics

Reporting groups

Reporting group title	Overall trial period
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Reporting group description: -

Reporting group values	Overall trial period	Total	
Number of subjects	58	58	
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)	58	58	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	36.4		
standard deviation	± 8.76	-	
Gender categorical			
Units: Subjects			
Female	27	27	
Male	31	31	
Height			
Units: meter			
arithmetic mean	1.748		
standard deviation	± 0.0737	-	
Weight			
Units: kilogram(s)			
arithmetic mean	76.53		
standard deviation	± 7.493	-	
BMI			
Units: kilogram(s)/square meter			
arithmetic mean	25.09		
standard deviation	± 2.486	-	
HbA1c			
Units: percent			
arithmetic mean	7.14		
standard deviation	± 0.539	-	
Duration of diabetes			
Units: years			
arithmetic mean	18.9		
standard deviation	± 9.17	-	

Subject analysis sets

Subject analysis set title	Group 2 subjects
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in group 2 treated with 0.3mg dasiglucagon and/or 0.5mg GlucaGen	
Subject analysis set title	Group 3 subjects
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in group 3 treated with 0.6 mg dasiglucagon and/or 1.0mg GlucaGen	
Subject analysis set title	Group 4 subjects
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in group 4 treated with 1.0mg dasiglucagon and/or 1.0mg GlucaGen. For summaries of PK and PD endpoints the data for 1.0 mg GlucaGen from groups 1, 3 and 4 were pooled.	
Subject analysis set title	Group 1 subjects
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in group 1 treated with 0.1 mg dasiglucagon or 1.0 mg GlucaGen	

Reporting group values	Group 2 subjects	Group 3 subjects	Group 4 subjects
Number of subjects	17	17	16
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	17	17	16
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	35.4	34.0	37.5
standard deviation	± 8.66	± 9.17	± 8.15
Gender categorical			
Units: Subjects			
Female	10	8	6
Male	7	9	10
Height			
Units: meter			
arithmetic mean	1.766	1.734	1.731
standard deviation	± 0.0721	± 0.0712	± 0.0857
Weight			
Units: kilogram(s)			
arithmetic mean	76.81	78.67	73.94
standard deviation	± 6.368	± 7.897	± 8.777
BMI			

Units: kilogram(s)/square meter arithmetic mean standard deviation	24.65 ± 1.945	26.21 ± 2.776	24.74 ± 2.962
HbA1c Units: percent arithmetic mean standard deviation	6.88 ± 0.494	7.24 ± 0.585	7.19 ± 0.571
Duration of diabetes Units: years arithmetic mean standard deviation	18.4 ± 10.28	19.2 ± 10.43	18.6 ± 5.29

Reporting group values	Group 1 subjects		
Number of subjects	8		
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)	8		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years arithmetic mean standard deviation	41.6 ± 8.31		
Gender categorical Units: Subjects			
Female	3		
Male	5		
Height Units: meter arithmetic mean standard deviation	1.771 ± 0.0491		
Weight Units: kilogram(s) arithmetic mean standard deviation	76.56 ± 5.494		
BMI Units: kilogram(s)/square meter arithmetic mean standard deviation	24.39 ± 0.960		
HbA1c Units: percent arithmetic mean standard deviation	7.41 ± 0.210		
Duration of diabetes			

Units: years			
arithmetic mean	19.9		
standard deviation	± 11.49		

End points

End points reporting groups

Reporting group title	Group 1 0.1 mg dasiglucagon
Reporting group description:	
Group 1 parallel design 0.1 mg dasiglucagon or 1.0 mg GlucaGen	
Reporting group title	Group 2 0.3 mg dasiglucagon
Reporting group description:	
Group 2 crossover design 0.3 mg dasiglucagon with 0.5 mg GlucaGen	
Reporting group title	Group 3 0.6 mg dasiglucagon
Reporting group description:	
Group 3 crossover design 0.6 mg dasiglucagon with 1.0 mg GlucaGen	
Reporting group title	Group 4 1.0 mg dasiglucagon
Reporting group description:	
Group 4 crossover design 1.0 mg dasiglucagon with 1.0 mg GlucaGen	
Reporting group title	Group 2 0.5 mg GlucaGen
Reporting group description:	
Group 2 crossover design 0.3 mg dasiglucagon with 0.5 mg GlucaGen	
Reporting group title	Group 3 1.0 mg GlucaGen
Reporting group description:	
Group 3 crossover design 0.6 mg dasiglucagon with 1.0 mg GlucaGen	
Reporting group title	Group 1 1.0 mg GlucaGen
Reporting group description:	
Group 1 parallel design 0.1 mg dasiglucagon or 1.0 mg GlucaGen	
Reporting group title	Group 4 1.0 mg GlucaGen
Reporting group description:	
Group 4 crossover design 1.0 mg dasiglucagon with 1.0 mg GlucaGen	
Subject analysis set title	Group 2 subjects
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in group 2 treated with 0.3mg dasiglucagon and/or 0.5mg GlucaGen	
Subject analysis set title	Group 3 subjects
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in group 3 treated with 0.6 mg dasiglucagon and/or 1.0mg GlucaGen	
Subject analysis set title	Group 4 subjects
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in group 4 treated with 1.0mg dasiglucagon and/or 1.0mg GlucaGen. For summaries of PK and PD endpoints the data for 1.0 mg GlucaGen from groups 1, 3 and 4 were pooled.	
Subject analysis set title	Group 1 subjects
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in group 1 treated with 0.1 mg dasiglucagon or 1.0 mg GlucaGen	

Primary: AUC(0-30min)

End point title	AUC(0-30min) ^[1]
End point description:	
Area under the plasma dasiglucagon or GlucaGen concentration vs. time curve from 0 to 30 min post-dose. The GlucaGen endpoints are displayed as derived from baseline-adjusted profiles.	
End point type	Primary

End point timeframe:

0-30min post dose

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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	16	16
Units: pmol*h/L				
geometric mean (geometric coefficient of variation)	95.4 (± 32.2)	292 (± 26.1)	413 (± 36.8)	833 (± 34.7)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[2]		
Units: pmol*h/L				
geometric mean (geometric coefficient of variation)	362 (± 27.8)	576 (± 29.9)		

Notes:

[2] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

Statistical analysis title	0.3mg dasiglucagon vs 0.5mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 2 0.3 mg dasiglucagon v Group 2 0.5 mg GlucaGen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[3]
P-value	= 0.0478
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	0.811
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.684
upper limit	0.9614

Notes:

[3] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 16 received dasiglucagon and 17 received

Statistical analysis title	0.6mg dasiglucagon vs 1.0mg GlucaGen
Statistical analysis description:	
Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.	
Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.	
Comparison groups	Group 3 0.6 mg dasiglucagon v Group 3 1.0 mg GlucaGen
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[4]
P-value	= 0.0315
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	0.789
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.6628
upper limit	0.9397

Notes:

[4] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 16 subjects were included in the analysis: 16 received dasiglucagon and 16 received GlucaGen. The group had a crossover design.

Statistical analysis title	1.0mg dasiglucagon vs 1.0mg GlucaGen
Statistical analysis description:	
Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.	
Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.	
Comparison groups	Group 4 1.0 mg dasiglucagon v Group 3 1.0 mg GlucaGen
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[5]
P-value	= 0.0217
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.0883
upper limit	1.5577

Notes:

[5] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. This was actually a comparison of Group 4 1.0 mg dasiglucagon and Group 4 1.0 mg GlucaGen. Number of subjects in this analysis was 16 (16 received dasiglucagon and 15 received

GlucaGen). The group had a crossover design.

Primary: AUC(0-360min)

End point title	AUC(0-360min) ^[6]
End point description:	
Area under the plasma dasiglucagon or GlucaGen concentration vs. time curve from 0 to 360 min post-dose. The GlucaGen endpoints are displayed as derived from baseline-adjusted profiles.	
End point type	Primary
End point timeframe:	
0-360 min post dose	

Notes:

[6] - 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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	16	16
Units: pmol*h/L				
geometric mean (geometric coefficient of variation)	437 (± 27.4)	1350 (± 12.2)	2610 (± 14.0)	4740 (± 14.5)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[7]		
Units: pmol*h/L				
geometric mean (geometric coefficient of variation)	924 (± 18.8)	1630 (± 19.0)		

Notes:

[7] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

Statistical analysis title	0.3mg dasiglucagon vs 0.5mg Glucagen
Statistical analysis description:	
Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.	
Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.	
Comparison groups	Group 2 0.3 mg dasiglucagon v Group 2 0.5 mg GlucaGen

Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[8]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.47
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.3774
upper limit	1.575

Notes:

[8] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 16 received dasiglucagon and 17 received GlucaGen. The group had a crossover design.

Statistical analysis title	0.6mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 0.6 mg dasiglucagon v Group 3 1.0 mg GlucaGen
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[9]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.76
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.5774
upper limit	1.967

Notes:

[9] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 16 subjects were included in the analysis: 16 received dasiglucagon and 16 received GlucaGen. The group had a crossover design.

Statistical analysis title	1.0mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 1.0 mg GlucaGen v Group 4 1.0 mg dasiglucagon
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Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[10]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	2.66
Confidence interval	
level	90 %
sides	2-sided
lower limit	2.5224
upper limit	2.8056

Notes:

[10] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. This was actually a comparison of Group 4 1.0 mg dasiglucagon and Group 4 1.0 mg GlucaGen. Number of subjects in this analysis was 16 (16 received dasiglucagon and 15 received GlucaGen). The group had a crossover design.

Primary: Cmax

End point title	Cmax ^[11]
End point description:	Maximum of all valid plasma dasiglucagon or GlucaGen concentration measurements from 0 to 360 min post-dose. The GlucaGen endpoints are displayed as derived from baseline-adjusted profiles.
End point type	Primary
End point timeframe:	0-360 min post dose

Notes:

[11] - 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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	16	16
Units: pmol/L				
geometric mean (geometric coefficient of variation)	320 (± 33.7)	954 (± 21.3)	1510 (± 28.2)	2690 (± 27.4)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[12]		
Units: pmol/L				
geometric mean (geometric coefficient of variation)	1060 (± 28.0)	1650 (± 30.6)		

Notes:

[12] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

Statistical analysis title	0.3mg dasiglucagon vs 0.5mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 2 0.3 mg dasiglucagon v Group 2 0.5 mg GlucaGen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[13]
P-value	= 0.1217
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	0.907
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8167
upper limit	1.0068

Notes:

[13] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 16 received dasiglucagon and 17 received GlucaGen. The group had a crossover design.

Statistical analysis title	0.6mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 0.6 mg dasiglucagon v Group 3 1.0 mg GlucaGen
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[14]
P-value	= 0.7359
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.03
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.885
upper limit	1.1991

Notes:

[14] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 16 subjects were included in the analysis: 16 received dasiglucagon and 16 received GlucaGen. The group had a crossover design.

Statistical analysis title	1.0mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 1.0 mg GlucaGen v Group 4 1.0 mg dasiglucagon
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[15]
P-value	= 0.0002
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.44
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.2679
upper limit	1.6332

Notes:

[15] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. This was actually a comparison of Group 4 1.0 mg dasiglucagon and Group 4 1.0 mg GlucaGen. Number of subjects in this analysis was 16 (16 received dasiglucagon and 15 received GlucaGen). The group had a crossover design.

Primary: Tmax

End point title	Tmax ^[16]
End point description:	Time to maximum of plasma dasiglucagon or GlucaGen concentration measurements. The GlucaGen endpoints are displayed as derived from baseline-adjusted profiles.
End point type	Primary
End point timeframe:	0-360 min post dose

Notes:

[16] - 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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	16	16
Units: hours				
median (full range (min-max))	0.500 (0.500 to 0.583)	0.625 (0.333 to 0.833)	0.583 (0.500 to 1.67)	0.625 (0.333 to 0.833)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[17]		

Units: hours				
median (full range (min-max))	0.250 (0.167 to 0.583)	0.333 (0.167 to 0.833)		

Notes:

[17] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

Statistical analysis title	0.3mg dasiglucagon vs 0.5mg Glucagen
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Statistical analysis description:

As tmax was a discontinuous parameter, it was analysed using Wilcoxon's Signed Rank test for paired observations within each group in a non-parametric analysis. Point estimates of median differences between treatments were determined according to Hodges and Lehmann, together with the corresponding 90% confidence intervals.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 2 0.5 mg GlucaGen v Group 2 0.3 mg dasiglucagon
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[18]
P-value	= 0.0009
Method	Wilcoxon's Signed Rank test
Parameter estimate	Median difference (final values)
Point estimate	0.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.1667
upper limit	0.4167

Notes:

[18] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 16 received dasiglucagon and 17 received GlucaGen. The group had a crossover design.

Statistical analysis title	0.6mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

As tmax was a discontinuous parameter, it was analysed using Wilcoxon's Signed Rank test for paired observations within each group in a non-parametric analysis. Point estimates of median differences between treatments were determined according to Hodges and Lehmann, together with the corresponding 90% confidence intervals.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 0.6 mg dasiglucagon v Group 3 1.0 mg GlucaGen
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[19]
P-value	< 0.0001
Method	Wilcoxon's Signed Rank test
Parameter estimate	Median difference (final values)
Point estimate	0.333

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.25
upper limit	0.5

Notes:

[19] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 16 subjects were included in the analysis: 16 received dasiglucagon and 16 received GlucaGen. The group had a crossover design.

Statistical analysis title	1.0mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

As tmax was a discontinuous parameter, it was analysed using Wilcoxon's Signed Rank test for paired observations within each group in a non-parametric analysis. Point estimates of median differences between treatments were determined according to Hodges and Lehmann, together with the corresponding 90% confidence intervals.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 1.0 mg GlucaGen v Group 4 1.0 mg dasiglucagon
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[20]
P-value	= 0.002
Method	Wilcoxon's Signed Rank test
Parameter estimate	Median difference (final values)
Point estimate	0.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.1667
upper limit	0.3333

Notes:

[20] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. This was actually a comparison of Group 4 1.0 mg dasiglucagon and Group 4 1.0 mg GlucaGen. Number of subjects in this analysis was 16 (16 received dasiglucagon and 15 received GlucaGen). The group had a crossover design.

Primary: λ_z

End point title	λ_z ^{[21][22]}
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End point description:

Terminal elimination rate constant of plasma dasiglucagon or GlucaGen. The GlucaGen endpoints are displayed as derived from baseline-adjusted profiles.

End point type	Primary
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End point timeframe:

0-360 min post dose

Notes:

[21] - 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: As there were multiple primary PK endpoints, λ_z was analysed using summary statistics by treatment and dose. No ANOVA was performed.

[22] - 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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	16	16
Units: h-1				
geometric mean (geometric coefficient of variation)	1.63 (± 19.6)	1.64 (± 18.5)	1.46 (± 22.2)	1.35 (± 30.0)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[23]		
Units: h-1				
geometric mean (geometric coefficient of variation)	1.90 (± 19.2)	1.73 (± 26.9)		

Notes:

[23] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

No statistical analyses for this end point

Primary: T_{1/2}

End point title	T _{1/2} ^{[24][25]}
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End point description:

Terminal plasma elimination half-life of dasiglucagon or GlucaGen. The GlucaGen endpoints are displayed as derived from baseline-adjusted profiles.

End point type	Primary
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End point timeframe:

0-360 min post dose

Notes:

[24] - 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: As there were multiple primary PK endpoints, T_{1/2} was analysed using summary statistics by treatment and dose. No ANOVA was performed.

[25] - 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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	16	16
Units: hours				
geometric mean (geometric coefficient of variation)	0.424 (± 20.3)	0.423 (± 16.9)	0.475 (± 27.7)	0.515 (± 31.4)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[26]		
Units: hours				
geometric mean (geometric coefficient of variation)	0.364 (± 18.4)	0.401 (± 31.4)		

Notes:

[26] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

No statistical analyses for this end point

Primary: CL/f

End point title	CL/f ^[27] ^[28]
End point description:	
Total body clearance of plasma dasiglucagon or GlucaGen. The GlucaGen endpoints are displayed as derived from baseline-adjusted profiles.	
End point type	Primary
End point timeframe:	
0-360 min post dose	

Notes:

[27] - 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: As there were multiple primary PK endpoints, CL/f was analysed using summary statistics by treatment and dose. No ANOVA was performed.

[28] - 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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	16	16
Units: L/h				
geometric mean (geometric coefficient of variation)	67.8 (± 30.0)	65.6 (± 12.0)	68.0 (± 14.8)	62.2 (± 16.7)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[29]		
Units: L/h				
geometric mean (geometric coefficient of variation)	163 (± 17.4)	180 (± 22.9)		

Notes:

[29] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

No statistical analyses for this end point

Primary: Vz/f

End point title	Vz/f ^{[30][31]}
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End point description:

Volume of distribution of plasma dasiglucagon or GlucaGen. The GlucaGen endpoints are displayed as derived from baseline-adjusted profiles.

End point type	Primary
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End point timeframe:

0-360 min post dose

Notes:

[30] - 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: As there were multiple primary PK endpoints, Vz/f was analysed using summary statistics by treatment and dose. No ANOVA was performed.

[31] - 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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	16	16
Units: Litres				
geometric mean (geometric coefficient of variation)	41.5 (± 41.8)	40.1 (± 21.2)	46.6 (± 39.5)	46.2 (± 36.6)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[32]		
Units: Litres				
geometric mean (geometric coefficient of variation)	85.5 (± 26.6)	104 (± 38.0)		

Notes:

[32] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

No statistical analyses for this end point

Primary: MRT

End point title	MRT ^[33] ^[34]
End point description: Mean residence time of plasma dasiglucagon or GlucaGen. The GlucaGen endpoints are displayed as derived from baseline-adjusted profiles.	
End point type	Primary
End point timeframe: 0-360 min post dose	

Notes:

[33] - 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: As there were multiple primary PK endpoints, MRT was analysed using summary statistics by treatment and dose. No ANOVA was performed.

[34] - 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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	16	16
Units: Hours				
geometric mean (geometric coefficient of variation)	1.05 (± 12.2)	1.07 (± 14.1)	1.29 (± 23.6)	1.29 (± 21.5)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[35]		
Units: Hours				
geometric mean (geometric coefficient of variation)	0.739 (± 13.9)	0.827 (± 20.4)		

Notes:

[35] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

No statistical analyses for this end point

Primary: AUE0-30min

End point title	AUE0-30min ^[36]
End point description: Area under the plasma glucose concentration vs. time curve from 0 to 30 min post-dose above baseline	
End point type	Primary
End point timeframe: 0-30 min post dose	

Notes:

[36] - 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.

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	17	16
Units: mg*h/dL				
arithmetic mean (standard deviation)	12.9 (± 5.21)	20.9 (± 6.13)	21.1 (± 6.10)	24.1 (± 5.18)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[37]		
Units: mg*h/dL				
arithmetic mean (standard deviation)	22.1 (± 5.48)	21.9 (± 5.74)		

Notes:

[37] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

Statistical analysis title	0.3mg dasiglucagon vs 0.5mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 2 0.3 mg dasiglucagon v Group 2 0.5 mg GlucaGen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[38]
P-value	= 0.4396
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	0.934
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8042
upper limit	1.0858

Notes:

[38] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 16 received dasiglucagon and 17 received GlucaGen. The group had a crossover design.

Statistical analysis title	0.6mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 0.6 mg dasiglucagon v Group 3 1.0 mg GlucaGen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[39]
P-value	= 0.596
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	0.965
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8613
upper limit	1.0822

Notes:

[39] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 17 received dasiglucagon and 16 received GlucaGen. The group had a crossover design.

Statistical analysis title	1.0mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 1.0 mg GlucaGen v Group 4 1.0 mg dasiglucagon
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[40]
P-value	= 0.1507
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.11
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9833
upper limit	1.2556

Notes:

[40] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. This was actually a comparison of Group 4 1.0 mg dasiglucagon and Group 4 1.0 mg GlucaGen. 16 subjects were included in the analysis: 16 received dasiglucagon and 15 received GlucaGen. The group had a crossover design.

Primary: AUE

End point title	AUE ^[41]
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End point description:

Area under the plasma glucose concentration vs. time curve from 0 to last available measurement post-dose above baseline

End point type	Primary
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End point timeframe:

0-360 min post dose

Notes:

[41] - 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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	17	16
Units: mg*h/dL				
arithmetic mean (standard deviation)	344 (± 149)	666 (± 247)	788 (± 165)	895 (± 213)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[42]		
Units: mg*h/dL				
arithmetic mean (standard deviation)	462 (± 273)	566 (± 232)		

Notes:

[42] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

Statistical analysis title	0.3mg dasiglucagon vs 0.5mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 2 0.3 mg dasiglucagon v Group 2 0.5 mg GlucaGen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[43]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.61
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.396
upper limit	1.8564

Notes:

[43] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 16 received dasiglucagon and 17 received GlucaGen. The group had a crossover design.

Statistical analysis title	0.6mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 0.6 mg dasiglucagon v Group 3 1.0 mg GlucaGen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[44]
P-value	= 0.0043
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.38
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.1676
upper limit	1.6303

Notes:

[44] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 17 received dasiglucagon and 16 received GlucaGen. The group had a crossover design.

Statistical analysis title	1.0mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 1.0 mg GlucaGen v Group 4 1.0 mg dasiglucagon
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[45]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.5649
upper limit	2.0043

Notes:

[45] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. This was actually a comparison of Group 4 1.0 mg dasiglucagon and Group 4 1.0 mg GlucaGen. 16 subjects were included in the analysis: 16 received dasiglucagon and 15 received GlucaGen. The group had a crossover design.

Primary: CE30min

End point title	CE30min ^[46]
End point description:	
Plasma glucose concentration at 30 min post-dose above baseline	
End point type	Primary
End point timeframe:	
0-30 min post dose	

Notes:

[46] - 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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	17	16
Units: mg/dL				
arithmetic mean (standard deviation)	66.1 (± 23.8)	93.4 (± 23.7)	98.2 (± 25.0)	100 (± 20.3)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[47]		
Units: mg/dL				
arithmetic mean (standard deviation)	93.5 (± 21.4)	96.5 (± 21.9)		

Notes:

[47] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

Statistical analysis title	0.3mg dasiglucagon vs 0.5mg Glucagen
Statistical analysis description:	
Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.	
Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.	
Comparison groups	Group 2 0.3 mg dasiglucagon v Group 2 0.5 mg GlucaGen

Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[48]
P-value	= 0.9195
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8933
upper limit	1.1353

Notes:

[48] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 16 received dasiglucagon and 17 received GlucaGen. The group had a crossover design.

Statistical analysis title	0.6mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 0.6 mg dasiglucagon v Group 3 1.0 mg GlucaGen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[49]
P-value	= 0.8449
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9255
upper limit	1.102

Notes:

[49] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 17 received dasiglucagon and 16 received GlucaGen. The group had a crossover design.

Statistical analysis title	1.0mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 1.0 mg GlucaGen v Group 4 1.0 mg dasiglucagon
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Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[50]
P-value	= 0.2366
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.06
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9767
upper limit	1.143

Notes:

[50] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. This was actually a comparison of Group 4 1.0 mg dasiglucagon and Group 4 1.0 mg GlucaGen. 16 subjects were included in the analysis: 16 received dasiglucagon and 15 received GlucaGen. The group had a crossover design.

Primary: CE

End point title	CE ^[51]
End point description:	
Maximum of all valid plasma glucose concentration measurements from 0 to 360 min post-dose above baseline	
End point type	Primary
End point timeframe:	
0-360 min post dose	

Notes:

[51] - 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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	17	16
Units: mg/dL				
arithmetic mean (standard deviation)	102 (± 33.7)	174 (± 44.6)	190 (± 32.2)	209 (± 40.2)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[52]		
Units: mg/dL				
arithmetic mean (standard deviation)	142 (± 42.6)	166 (± 42.5)		

Notes:

[52] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

Statistical analysis title	0.3mg dasiglucagon vs 0.5mg Glucagen
Statistical analysis description:	
Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.	
Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.	
Comparison groups	Group 2 0.3 mg dasiglucagon v Group 2 0.5 mg GlucaGen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[53]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.24
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.1604
upper limit	1.3242

Notes:

[53] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 16 received dasiglucagon and 17 received GlucaGen. The group had a crossover design.

Statistical analysis title	0.6mg dasiglucagon vs 1.0mg Glucagen
Statistical analysis description:	
Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.	
Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.	
Comparison groups	Group 3 0.6 mg dasiglucagon v Group 3 1.0 mg GlucaGen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[54]
P-value	= 0.0305
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.14
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.0353
upper limit	1.2513

Notes:

[54] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 17 received dasiglucagon and 16 received GlucaGen. The group had a crossover design.

Statistical analysis title	1.0mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

Analysis of variance (ANOVA) with log-transformed response, treatment, period, sequence and patient within sequence as fixed effect. The ratio of geometric LS-means of treatments (ZP4207/GlucaGen) is presented within each group.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 1.0 mg GlucaGen v Group 4 1.0 mg dasiglucagon
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[55]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	least squares mean ratio
Point estimate	1.32
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.2174
upper limit	1.4271

Notes:

[55] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. This was actually a comparison of Group 4 1.0 mg dasiglucagon and Group 4 1.0 mg GlucaGen. 16 subjects were included in the analysis: 16 received dasiglucagon and 15 received GlucaGen. The group had a crossover design.

Primary: Glucose tmax

End point title	Glucose tmax ^[56]
End point description:	
Time to maximum of plasma glucose concentration measurements	
End point type	Primary
End point timeframe:	
0-360 min post dose	

Notes:

[56] - 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: GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

End point values	Group 1 0.1 mg dasiglucagon	Group 2 0.3 mg dasiglucagon	Group 3 0.6 mg dasiglucagon	Group 4 1.0 mg dasiglucagon
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	16	17	16
Units: hours				
median (full range (min-max))	1.25 (0.833 to 1.67)	1.67 (1.00 to 2.50)	1.67 (1.67 to 4.33)	2.50 (1.67 to 2.50)

End point values	Group 2 0.5 mg GlucaGen	Group 3 1.0 mg GlucaGen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	16 ^[57]		
Units: hours				

median (full range (min-max))	1.00 (0.667 to 5.00)	1.25 (0.833 to 6.12)		
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Notes:

[57] - Number of subjects was 33 as GlucaGen 1.0 mg data available for Groups 1, 3 and 4 were pooled

Statistical analyses

Statistical analysis title	0.3mg dasiglucagon vs 0.5mg Glucagen
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Statistical analysis description:

As glucose tmax was a discontinuous parameter, it was analysed using Wilcoxon's Signed Rank test for paired observations within each group in a non-parametric analysis. Point estimates of median differences between treatments were determined according to Hodges and Lehmann, together with the corresponding 90% confidence intervals.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 2 0.3 mg dasiglucagon v Group 2 0.5 mg GlucaGen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[58]
P-value	= 0.0085
Method	Wilcoxon's Signed Rank test
Parameter estimate	Median difference (final values)
Point estimate	0.667
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.4167
upper limit	0.667

Notes:

[58] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 16 received dasiglucagon and 17 received GlucaGen. The group had a crossover design.

Statistical analysis title	0.6mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

As glucose tmax was a discontinuous parameter, it was analysed using Wilcoxon's Signed Rank test for paired observations within each group in a non-parametric analysis. Point estimates of median differences between treatments were determined according to Hodges and Lehmann, together with the corresponding 90% confidence intervals.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 0.6 mg dasiglucagon v Group 3 1.0 mg GlucaGen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	equivalence ^[59]
P-value	= 0.0508
Method	Wilcoxon's Signed Rank test
Parameter estimate	Median difference (final values)
Point estimate	0.417

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.4167
upper limit	0.8333

Notes:

[59] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. 17 subjects were included in the analysis: 17 received dasiglucagon and 16 received GlucaGen. The group had a crossover design.

Statistical analysis title	1.0mg dasiglucagon vs 1.0mg Glucagen
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Statistical analysis description:

As glucose tmax was a discontinuous parameter, it was analysed using Wilcoxon's Signed Rank test for paired observations within each group in a non-parametric analysis. Point estimates of median differences between treatments were determined according to Hodges and Lehmann, together with the corresponding 90% confidence intervals.

Please note that the results are of an exploratory nature since there was no formal sample size calculation and no H0-hypothesis was defined.

Comparison groups	Group 3 1.0 mg GlucaGen v Group 4 1.0 mg dasiglucagon
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence ^[60]
P-value	< 0.0001
Method	Wilcoxon's Signed Rank test
Parameter estimate	Median difference (final values)
Point estimate	1.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.8333
upper limit	1.25

Notes:

[60] - Treatments may be described as comparable if the 90% CI of the respective ratio was within the interval of 0.8-1.25. A formal test of equivalence was not performed, the p-value is from an exploratory superiority test. This was actually a comparison of Group 4 1.0 mg dasiglucagon and Group 4 1.0 mg GlucaGen. 16 subjects were included in the analysis: 16 received dasiglucagon and 15 received GlucaGen. The group had a crossover design.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the time of the first trial related activity after the patient signed the informed consent until the follow-up visit at end of trial. Reporting will be on treatment emergent adverse events only.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	0.1 mg dasiglucagon
Reporting group description:	
0.1 mg dasiglucagon	
Reporting group title	0.3 mg dasiglucagon
Reporting group description:	
0.3 mg dasiglucagon	
Reporting group title	0.6 mg dasiglucagon
Reporting group description:	
0.6 mg dasiglucagon	
Reporting group title	1.0 mg dasiglucagon
Reporting group description:	
1.0 mg dasiglucagon	
Reporting group title	0.5 mg GlucaGen
Reporting group description:	
0.5 mg GlucaGen	
Reporting group title	1.0 mg GlucaGen
Reporting group description:	
1.0 mg GlucaGen	

Serious adverse events	0.1 mg dasiglucagon	0.3 mg dasiglucagon	0.6 mg dasiglucagon
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	1.0 mg dasiglucagon	0.5 mg GlucaGen	1.0 mg GlucaGen
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 34 (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: 5 %

Non-serious adverse events	0.1 mg dasiglucagon	0.3 mg dasiglucagon	0.6 mg dasiglucagon
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	10 / 16 (62.50%)	11 / 17 (64.71%)
Vascular disorders			
Cardiovascular insufficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Orthostatic intolerance			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Head discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	3 / 6 (50.00%)	6 / 16 (37.50%)	5 / 17 (29.41%)
occurrences (all)	3	8	6
Vertigo			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Burning sensation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Injection site erythema			
subjects affected / exposed	1 / 6 (16.67%)	1 / 16 (6.25%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Injection site oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Injection site pruritus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 16 (6.25%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Injection site urticaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Mucosal erosion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	9 / 16 (56.25%)	9 / 17 (52.94%)
occurrences (all)	1	9	9
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	6 / 16 (37.50%)	6 / 17 (35.29%)
occurrences (all)	0	6	6
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 16 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 16 (6.25%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hypoglycaemia	Additional description: The values reported exclude hypoglycemia events from the start of insulin-induced hypoglycemic procedure up to dosing.		
subjects affected / exposed	1 / 6 (16.67%)	0 / 16 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1

Non-serious adverse events	1.0 mg dasiglucagon	0.5 mg GlucaGen	1.0 mg GlucaGen
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 16 (68.75%)	10 / 17 (58.82%)	23 / 34 (67.65%)
Vascular disorders			
Cardiovascular insufficiency			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Orthostatic intolerance			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Palpitations			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	0 / 34 (0.00%) 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Head discomfort			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	5 / 16 (31.25%)	1 / 17 (5.88%)	7 / 34 (20.59%)
occurrences (all)	5	1	7
Vertigo			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Burning sensation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Fatigue			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Feeling hot			
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Hyperhidrosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	1 / 16 (6.25%)	0 / 17 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Injection site oedema			
subjects affected / exposed	2 / 16 (12.50%)	0 / 17 (0.00%)	2 / 34 (5.88%)
occurrences (all)	2	0	2
Injection site pruritus			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 17 (5.88%) 1	0 / 34 (0.00%) 0
Injection site urticaria subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	1 / 34 (2.94%) 1
Mucosal erosion subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 17 (5.88%) 1	0 / 34 (0.00%) 0
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 17 (0.00%) 0	0 / 34 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 17 (5.88%) 1	0 / 34 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	1 / 34 (2.94%) 1
Dysgeusia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 17 (0.00%) 0	0 / 34 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	1 / 34 (2.94%) 1
Nausea subjects affected / exposed occurrences (all)	7 / 16 (43.75%) 7	9 / 17 (52.94%) 9	18 / 34 (52.94%) 18
Vomiting subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	4 / 17 (23.53%) 5	4 / 34 (11.76%) 4
Respiratory, thoracic and mediastinal disorders			
Dyspnoea subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 17 (0.00%) 0	0 / 34 (0.00%) 0
Nasopharyngitis			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 17 (0.00%) 0	1 / 34 (2.94%) 1
Endocrine disorders Hypoglycaemia	Additional description: The values reported exclude hypoglycemia events from the start of insulin-induced hypoglycemic procedure up to dosing.		
subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	3 / 17 (17.65%) 3	5 / 34 (14.71%) 6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 January 2016	Administrative changes and minor clarifications

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported