



Clinical trial results:

A Randomized Trial in 2 Parts: Double-Blind, Placebo-Controlled, Crossover Part 1 and Open-label Part 2, Evaluating the Efficacy and Safety of Dasiglucagon for the Treatment of Children with Congenital Hyperinsulinism

Summary

EudraCT number	2017-004545-24
Trial protocol	DE GB
Global end of trial date	07 March 2022

Results information

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

Trial information

Trial identification

Sponsor protocol code	ZP4207-17103
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04172441
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Zealand Pharma A/S
Sponsor organisation address	Sydmarken 11, Soeborg, Denmark, 2860
Public contact	Clinical Operations, Zealand Pharma A/S, 45 88 77 36 00, clinicaltrials@zealandpharma.com
Scientific contact	Clinical Operations, Zealand Pharma A/S, 45 88 77 36 00, clinicaltrials@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	18 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 March 2022
Global end of trial reached?	Yes
Global end of trial date	07 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of dasiglucagon in reducing glucose requirements in children with persistent CHI requiring continuous IV glucose administration to prevent/manage hypoglycemia.

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	19 June 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 9
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Germany: 1
Worldwide total number of subjects	13
EEA total number of subjects	1

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	3
Infants and toddlers (28 days-23 months)	10
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This trial was conducted at a total of 4 sites; in the USA (2 sites), UK (1 site) and Germany (1 site).

Pre-assignment

Screening details:

A total of 16 patients were screened of which 13 patients were randomized. However, 1 patient was randomized in error and not treated.

Period 1

Period 1 title	Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	Dasiglucagon

Arm description:

Subjects in this arm received dasiglucagon continuous infusion via an infusion pump. Patients were randomly assigned in a double-blind fashion to receive dasiglucagon or placebo for 48 hours, after which they were crossed over to the other trial treatment for an additional 48 hours.

Arm type	Experimental
Investigational medicinal product name	dasiglucagon
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Dasiglucagon was administered via a subcutaneous infusion pump. The dose was titrated in a manner linked to the plasma glucose level achieved, and thus the dose varied between patients.

Arm title	Placebo
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Arm description:

Subjects in this arm received placebo. Patients were randomly assigned in a double-blind fashion to receive dasiglucagon or placebo for 48 hours, after which they were crossed over to the other trial treatment for an additional 48 hours.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

The placebo dose was titrated in a manner linked to the plasma glucose level achieved, and thus the dose varied between patients.

Number of subjects in period 1	Dasiglucagon	Placebo
Started	12	12
Completed	12	12

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Dasiglucagon
Arm description:	
Subjects received open-label treatment with dasiglucagon for 21 days.	
Arm type	Experimental
Investigational medicinal product name	dasiglucagon
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Dasiglucagon was administered via a subcutaneous infusion pump. The dose was titrated in a manner linked to the plasma glucose level achieved, and thus the dose varied between patients.

Number of subjects in period 2	Dasiglucagon
Started	12
Completed	12

Baseline characteristics

Reporting groups^[1]

Reporting group title	Period 1
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Reporting group description: -

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: Part 1 of the trial utilised a cross-over design. A total of 12 subject received both dasiglucagon and placebo in Part 1 of the trial.

Reporting group values	Period 1	Total	
Number of subjects	12	12	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	3	3	
Infants and toddlers (28 days-23 months)	9	9	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: days			
arithmetic mean	71.25		
standard deviation	± 84.976	-	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	2	2	

End points

End points reporting groups

Reporting group title	Dasiglucagon
Reporting group description: Subjects in this arm received dasiglucagon continuous infusion via an infusion pump. Patients were randomly assigned in a double-blind fashion to receive dasiglucagon or placebo for 48 hours, after which they were crossed over to the other trial treatment for an additional 48 hours.	
Reporting group title	Placebo
Reporting group description: Subjects in this arm received placebo. Patients were randomly assigned in a double-blind fashion to receive dasiglucagon or placebo for 48 hours, after which they were crossed over to the other trial treatment for an additional 48 hours.	
Reporting group title	Dasiglucagon
Reporting group description: Subjects received open-label treatment with dasiglucagon for 21 days.	

Primary: Mean IV GIR in the last 12 hours of each treatment period during Part 1

End point title	Mean IV GIR in the last 12 hours of each treatment period during Part 1
End point description: Mean Intravenous Glucose Infusion Rate in the last 12 hours of each treatment period during Part 1 (dasiglucagon or placebo administration).	
End point type	Primary
End point timeframe: Measured over the last 12-hour treatment period at the end of each of the cross-over treatment periods in Part 1, from 36h to 48 h and from 84h to 96h after the start of study treatment.	

End point values	Dasiglucagon	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: mg/kg/min				
arithmetic mean (standard deviation)	4.33 (± 4.922)	9.51 (± 5.655)		

Statistical analyses

Statistical analysis title	Primary Statistical Analysis
Statistical analysis description: The primary analysis was defined by the estimand based on the treatment policy (de-facto) strategy, where the actual GIR measurement reported irrespective of adherence to treatment or the use of subsequent therapy were used for the analysis . The difference in weighted mean IV GIR between placebo and dasiglucagon was estimated.	
Comparison groups	Dasiglucagon v Placebo

Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	= 0.0037
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.29
upper limit	-2.13

Notes:

[1] - Mixed model with treatment and period as fixed effects and patient as random effect.

Secondary: Total amount of carbohydrates administered per day during Part 1

End point title	Total amount of carbohydrates administered per day during Part 1
End point description:	Total amount (g) of carbohydrates administered (regardless of the route) per day during each of the 48-hour treatment periods in Part 1.
End point type	Secondary
End point timeframe:	Day 1 to 4, summarised for each 48-hour treatment period

End point values	Dasiglucagon	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: gram(s)				
arithmetic mean (standard deviation)	106.7 (± 53.72)	139.1 (± 57.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean IV GIR below 10 mg/kg/min in the last 12 hours of each treatment period during Part 1

End point title	Mean IV GIR below 10 mg/kg/min in the last 12 hours of each treatment period during Part 1
End point description:	The weighted mean intravenous (IV) Glucose Infusion Rate (GIR) <10 mg/kg/min over the last 12-hour treatment period of Part 1.
End point type	Secondary
End point timeframe:	Over the last 12-hour treatment period in the last treatment period of Part 1.

End point values	Dasiglucagon	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Subjects				
Less than 10 mg/kg/min	9	6		
Greater than or equal to 10 mg/kg/min	3	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to complete weaning off IV GIR

End point title	Time to complete weaning off IV GIR
End point description: Time to complete weaning off IV GIR (time from first exposure during Part 2 to stop of IV glucose infusion). Complete weaning off IV GIR was defined as the first point in time when the patient had been off IV GIR for 12 hours.	
End point type	Secondary
End point timeframe: From day 5-25.	

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects				
End of Week 1	7			
End of Week 2	10			
End of Week 3	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Hypoglycaemia event rate as detected by SMPG

End point title	Hypoglycaemia event rate as detected by SMPG
End point description: Hypoglycaemia event rate, defined as number of hypoglycaemic events (PG <70 mg/dL or 3.9 mmol/L), as detected by SMPG	
End point type	Secondary

End point timeframe:

Day 5 to 25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Hypoglycaemic events				
arithmetic mean (standard deviation)	9.47 (\pm 9.121)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically significant hypoglycaemia event rate as detected by SMPG

End point title	Clinically significant hypoglycaemia event rate as detected by SMPG
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End point description:

Clinically significant hypoglycaemia event rate, defined as number of events <54 mg/dL (3.0 mmol/L), as detected by SMPG

End point type	Secondary
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End point timeframe:

Day 5-25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Hypoglycaemic events				
arithmetic mean (standard deviation)	2.70 (\pm 3.641)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to actual hospital discharge

End point title	Time to actual hospital discharge
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End point description:

Time to actual hospital discharge, defined as the time from first exposure during Part 2 to discharge from hospital, presented as cumulative number of subjects with discharge per week.

End point type	Secondary
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End point timeframe:

Day 5-25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects				
End of Week 1	0			
End of Week 2	4			
End of Week 3	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to pancreatic surgery (sub-total or total pancreatectomy)

End point title	Time to pancreatic surgery (sub-total or total pancreatectomy)
End point description: Time to pancreatic surgery (sub-total or total pancreatectomy), presented by cumulative number of subjects receiving sub-total or total pancreatectomy (with a cutoff of $\geq 95\%$) by week.	
End point type	Secondary
End point timeframe: Day 5-25	

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Subjects				
End of Week 1	0			
End of Week 2	1			
End of Week 3	1			
End of Week 4	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Amount of Carbohydrates Administration - Total

End point title	Amount of Carbohydrates Administration - Total
End point description:	
End point type	Secondary

End point timeframe:

Day 5-25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: gram(s) per day				
arithmetic mean (standard deviation)				
Week 1	104.41 (\pm 38.927)			
Week 2	92.43 (\pm 50.278)			
Week 3	92.81 (\pm 58.265)			
Weeks 1-3	95.40 (\pm 40.723)			

Statistical analyses

No statistical analyses for this end point

Secondary: Amount of Carbohydrates Administration - IV Glucose or Total Parenteral Nutrition

End point title	Amount of Carbohydrates Administration - IV Glucose or Total Parenteral Nutrition
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End point description:

End point type	Secondary
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End point timeframe:

Day 5-25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: grams (g) per day				
arithmetic mean (standard deviation)				
Week 1	46.06 (\pm 33.155)			
Week 2	19.05 (\pm 29.637)			
Week 3	31.50 (\pm 51.174)			
Weeks 1-3	32.24 (\pm 27.569)			

Statistical analyses

No statistical analyses for this end point

Secondary: Amount of Carbohydrates Administration - Oral

End point title	Amount of Carbohydrates Administration - Oral
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End point description:

End point type	Secondary
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End point timeframe:

Day 5-25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: gram(s) per day				
arithmetic mean (standard deviation)				
Week 1	22.99 (± 24.033)			
Week 2	23.69 (± 33.582)			
Week 3	14.91 (± 21.554)			
Weeks 1-3	22.67 (± 25.099)			

Statistical analyses

No statistical analyses for this end point

Secondary: Amount of Carbohydrates Administration - NG-tube or Gastrostomy

End point title	Amount of Carbohydrates Administration - NG-tube or Gastrostomy
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End point description:

End point type	Secondary
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End point timeframe:

Day 5-25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: gram(s) per day				
arithmetic mean (standard deviation)				
Week 1	35.36 (± 28.788)			
Week 2	49.69 (± 26.597)			
Week 3	46.41 (± 26.820)			
Weeks 1-3	40.49 (± 25.836)			

Statistical analyses

No statistical analyses for this end point

Secondary: CGM percent time in range 70-180 mg/dL (3.9-10.0 mmol/L)

End point title	CGM percent time in range 70-180 mg/dL (3.9-10.0 mmol/L)
End point description:	
End point type	Secondary
End point timeframe:	
Day 5-25	

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: percent				
median (full range (min-max))				
Week 1	88.88 (34.5 to 94.3)			
Week 2	88.24 (51.0 to 95.9)			
Week 3	91.42 (36.3 to 100.0)			
Weeks 1-3	88.35 (42.5 to 100.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: CGM percent time in hypoglycemia (<70 mg/dL or 3.9 mmol/L)

End point title	CGM percent time in hypoglycemia (<70 mg/dL or 3.9 mmol/L)
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End point description:

End point type	Secondary
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End point timeframe:

Day 5-25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: percent				
median (full range (min-max))				
Week 1	7.05 (1.0 to 24.5)			
Week 2	7.35 (0.6 to 49.0)			
Week 3	5.73 (0.0 to 22.1)			
Weeks 1-3	6.67 (0.0 to 30.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: CGM percent time in clinically significant hypoglycaemia (<54 mg/dL or 3.0 mmol/L)

End point title	CGM percent time in clinically significant hypoglycaemia (<54 mg/dL or 3.0 mmol/L)
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End point description:

End point type	Secondary
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End point timeframe:

Day 5-25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: percent				
median (full range (min-max))				

Week 1	1.92 (0.2 to 6.0)			
Week 2	2.03 (0.0 to 20.4)			
Week 3	0.88 (0.0 to 6.9)			
Weeks 1-3	1.75 (0.0 to 9.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of hypoglycaemia episodes for 15 min or more, as measured by CGM

End point title	Rate of hypoglycaemia episodes for 15 min or more, as measured by CGM
End point description: Rate of hypoglycemia episodes, defined as number of episodes <70 mg/dL (3.9 mmol/L) for 15 min or more, as measured by CGM	
End point type	Secondary
End point timeframe: Day 5-25	

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Hypoglycaemic events				
median (full range (min-max))				
Week 1	22.00 (3.0 to 58.0)			
Week 2	26.00 (3.0 to 74.7)			
Week 3	18.63 (0.0 to 57.2)			
Weeks 1-3	18.54 (0.0 to 66.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of clinically significant hypoglycemia episodes for 15 min or more, as measured by CGM.

End point title	Rate of clinically significant hypoglycemia episodes for 15 min or more, as measured by CGM.
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End point description:

Rate of clinically significant hypoglycemia episodes, defined as number of episodes <54 mg/dL (3.0 mmol/L) for 15 min or more, as measured by CGM

End point type	Secondary
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End point timeframe:

Day 5-25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Hypoglycaemic episodes				
median (full range (min-max))				
Week 1	5.00 (1.0 to 23.0)			
Week 2	8.00 (0.0 to 46.7)			
Week 3	2.67 (0.0 to 18.7)			
Weeks 1-3	5.00 (0.0 to 34.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extent of hypoglycemia (area over the glucose curve [AOCglucose] below 70 mg/dL [3.9 mmol/L]) as measured by CGM

End point title	Extent of hypoglycemia (area over the glucose curve [AOCglucose] below 70 mg/dL [3.9 mmol/L]) as measured by CGM
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End point description:

Extent of hypoglycemia (area over the glucose curve [AOCglucose] below 70 mg/dL [3.9 mmol/L]) as measured by CGM

End point type	Secondary
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End point timeframe:

Day 5-25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: mmol/L				
median (full range (min-max))				
Week 1	0.04 (0.0 to 0.2)			
Week 2	0.05 (0.0 to 0.05)			

Week 3	0.03 (0.0 to 0.2)			
Weeks 1-3	0.05 (0.0 to 0.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Extent of clinically significant hypoglycaemia (AOCglucose below 54 mg/dL [3.0 mmol/L]) as measured by CGM

End point title	Extent of clinically significant hypoglycaemia (AOCglucose below 54 mg/dL [3.0 mmol/L]) as measured by CGM
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End point description:

End point type	Secondary
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End point timeframe:

Day 5-25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: mmol/L				
median (full range (min-max))				
Week 1	0.01 (0.0 to 0.01)			
Week 2	0.02 (0.0 to 0.1)			
Week 3	0.01 (0.0 to 0.01)			
Weeks 1-3	0.01 (0.0 to 0.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: CGM percent time in hyperglycaemia (>180 mg/dL or 10.0 mmol/L)

End point title	CGM percent time in hyperglycaemia (>180 mg/dL or 10.0 mmol/L)
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End point description:

End point type	Secondary
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End point timeframe:

Day 5-25

End point values	Dasiglucagon			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: percent				
median (full range (min-max))				
Week 1	1.44 (0.0 to 64.5)			
Week 2	0.15 (0.0 to 45.0)			
Week 3	0.32 (0.0 to 62.7)			
Weeks 1-3	0.78 (0.0 to 56.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the trial.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Dasiglucagon - Part 1
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Reporting group description:

Subjects in this arm received dasiglucagon continuous infusion via an infusion pump.

Reporting group title	Placebo - Part 1
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Reporting group description:

Subjects in this arm received placebo.

Reporting group title	Dasiglucagon - Part 2
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Reporting group description:

AEs occurring in Part 2 of the trial.

Serious adverse events	Dasiglucagon - Part 1	Placebo - Part 1	Dasiglucagon - Part 2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Dasiglucagon - Part 1	Placebo - Part 1	Dasiglucagon - Part 2
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 12 (25.00%)	7 / 12 (58.33%)	10 / 12 (83.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Haemangioma of liver subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Vascular disorders Thrombophlebitis Superficial subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1	0 / 12 (0.00%) 0
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Face oedema subjects affected / exposed occurrences (all) Medical device site reaction subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	2 / 12 (16.67%) 2 1 / 12 (8.33%) 1 1 / 12 (8.33%) 1
Respiratory, thoracic and mediastinal disorders Tachypnoea subjects affected / exposed occurrences (all) Pulmonary oedema subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1 0 / 12 (0.00%) 0	1 / 12 (8.33%) 1 1 / 12 (8.33%) 1	1 / 12 (8.33%) 1 0 / 12 (0.00%) 0
Product issues Device occlusion subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Investigations Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 12 (8.33%) 1	2 / 12 (16.67%) 2

Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 12 (8.33%) 1	1 / 12 (8.33%) 1
Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1	1 / 12 (8.33%) 1
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Normocytic anaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	3 / 12 (25.00%) 4 1 / 12 (8.33%) 1
Eye disorders Dry eye subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Haematochezia	1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0	1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0	2 / 12 (16.67%) 2 2 / 12 (16.67%) 2 2 / 12 (16.67%) 2 1 / 12 (8.33%) 1

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Rash papular			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	0	3
Dermatitis diaper			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Acne infantile			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Sensitive skin			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			

Finger deformity subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0
Infections and infestations			
Device related sepsis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Eye infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Fungal skin infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 2
Oral candidiasis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Parainfluenzae virus infection subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Rash pustular subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Metabolism and nutrition disorders			
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1	2 / 12 (16.67%) 3
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	2 / 12 (16.67%) 4
Acidosis hyperchloraemic subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Fluid retention subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1
Hypochloraemia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Hypophosphataemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2020	Dexcom G4 was changed to Dexcom G6 as the G4 was being phased out. Statistical section was updated focusing on the key secondary analysis description; the endpoint was rewritten to match the description in the endpoint section Pharmacokinetics/drug exposure section was updated: Visit 5 corrected to Day 5
04 June 2021	Updates to the secondary endpoints. Statistical section was updated with the updated endpoints. The safety section was clarified further.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported