Clinical trial results:
Assessment of Intranasal Glucagon in Children and Adolescents with Type 1 Diabetes

Summary

EudraCT number	2015-003252-40
Trial protocol	Outside EU/EEA
Global end of trial date	13 January 2015

Results information

Result version number	v2 (current)
This version publication date	04 July 2018
First version publication date	22 October 2017
Version creation reason	• Correction of full data set Data Correction

Trial information

Trial identification

Sponsor protocol code	16418

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01997411
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Alias: I8R-MC-IGBB, Additional Trial Identifier: AMG103

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5 PM EST , Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST , Eli Lilly and Company, 1 877-285-4559,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001657-PIP01-14
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	13 January 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 January 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to assess how glucagon administered nasally, using a nasal dosing delivery device, works in children and adolescents compared with commercially-available glucagon given by injection. In addition, the safety and tolerability of glucagon given nasally was evaluated.

Protection of trial subjects:

Guidelines as drawn up by the institutional review board were followed with regard to the treatment of human subjects in the study. These guidelines meet the requirements of the Declaration of Helsinki; they also meet the requirements of the United States Code of Federal Regulations (Title 21, Part 56), the Directive 2001/20/EC (Europe) and the Tri-Council Policy Statement (Canada). This study was performed in compliance with Good Clinical Practice.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	12 December 2013
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	United States: 48
Worldwide total number of subjects	48
EEA total number of subjects	0

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)	36
Adolescents (12-17 years)	12
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No Text Entered

Pre-assignment

Screening details:

No Text Entered

Period 1

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

Blinding implementation details:

IM and NG arms are open labeled. NG cohorts, 2mg and 3mg, are double blinded.

Arms

Are arms mutually exclusive?	No
Arm title	4 to<8 Years Old Intramuscular (IM) Glucagon Visit

Arm description:

This was completed at one visit and was the only visit for this cohort.

Arm type	Active comparator
Investigational medicinal product name	Intramuscular Glucagon
Investigational medicinal product code	
Other name	Glucagon, GlucaGen HypoKit
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants who weighed at least 25 kilograms (kg)/55 pounds (lbs) were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 lbs, IM glucagon dosed with 0.5 mg.

Arm title	4 to <8 Years Old NG 2.0 mg 1st Visit/3.0 mg 2nd Visit

Arm description:

At the first visit, a nasal glucagon (NG) dose of 2.0 milligrams (mg) for participants 4 to less than 8 years of age was administered nasally.

At the second visit, NG dose of 3.0 mg was administered nasally.

Arm type	Experimental
Investigational medicinal product name	Nasal Glucagon (NG)
Investigational medicinal product code	
Other name	Dry-Mist nasal glucagon, AMG504-1, LY900018
Pharmaceutical forms	Nasal powder
Routes of administration	Nasal use

Dosage and administration details:

NG doses of 2.0 mg and 3.0 mg for participants 4 to less than 8 years of age were administered in a nostril with a prefilled delivery device that delivered a single dose upon activation.

Arm title	4 to <8 Years Old NG 3.0 mg 1st Visit/2.0 mg 2nd Visit

Arm description:

At the first visit, a NG dose of 3.0 mg for participants 4 to less than 8 years of age was administered nasally.

At the second visit, a NG dose of 2.0 mg was administered nasally.

Arm type	Experimental
Investigational medicinal product name	Nasal Glucagon (NG)
Investigational medicinal product code	
Other name	Dry-Mist nasal glucagon, AMG504-1, LY900018
Pharmaceutical forms	Nasal powder
Routes of administration	Nasal use

Dosage and administration details:

NG doses of 3.0 mg and 2.0 mg for participants 4 to less than 8 years of age were administered in a nostril with a prefilled delivery device that delivered a single dose upon activation.

Arm title	8 to <12 Years Old Intramuscular Glucagon Visit

Arm description:

This was completed at one visit and was the only "dosing" visit for this cohort.

Arm type	Active comparator
Investigational medicinal product name	Intramuscular Glucagon
Investigational medicinal product code	
Other name	Glucagon, GlucaGen HypoKit
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 lbs, IM glucagon dosed with 0.5 mg.

Arm title	8 to <12 Years Old NG 2.0 mg 1st Visit/3.0 mg 2nd Visit

Arm description:

At the first visit, a NG dose of 2.0 mg for participants 8 to less than 12 years of age was administered nasally.

At the second visit, a NG dose of 3.0 mg was administered nasally.

Arm type	Experimental
Investigational medicinal product name	Nasal Glucagon (NG)
Investigational medicinal product code	
Other name	Dry-Mist nasal glucagon, AMG504-1, LY900018
Pharmaceutical forms	Nasal powder
Routes of administration	Nasal use

Dosage and administration details:

NG doses of 2.0 mg and 3.0 mg for participants 8 to less than 12 years of age were administered in a nostril with a prefilled delivery device that delivered a single dose upon activation.

Arm title	8 to <12 Years Old NG 3.0 mg 1st Visit/2.0 mg 2nd Visit

Arm description:

At the first visit, a NG dose of 3.0 mg for participants 8 to less than 12 years of age was administered nasally.

At the second visit, a NG dose of 2.0 mg was administered nasally.

Arm type	Experimental
Investigational medicinal product name	Nasal Glucagon (NG)
Investigational medicinal product code	
Other name	Dry-Mist nasal glucagon, AMG504-1, LY900018
Pharmaceutical forms	Nasal powder
Routes of administration	Nasal use

Dosage and administration details:

NG doses of 3.0 mg and 2.0 mg for participants 8 to less than 12 years of age were administered in a nostril with a prefilled delivery device that delivered a single dose upon activation.

Arm title	12 to <17 Years Old NG 3.0 mg 1st Visit/IM Glucagon 2nd Visit

Arm description:

At the first visit, a NG dose of 3.0 mg was administered nasally.

At the second visit, participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 Ibs, IM glucagon dose was 0.5 mg.

Arm type	Experimental
Investigational medicinal product name	Nasal Glucagon (NG)
Investigational medicinal product code	
Other name	Dry-Mist nasal glucagon, AMG504-1, LY900018
Pharmaceutical forms	Nasal powder
Routes of administration	Nasal use

Dosage and administration details:

NG doses of 3.0 mg for those 12 to less than 17 years of age were administered in a nostril with a prefilled delivery device that
delivered a single dose upon activation.

Investigational medicinal product name	Intramuscular Glucagon
Investigational medicinal product code	
Other name	Glucagon, GlucaGen HypoKit
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 lbs, IM glucagon dosed with 0.5 mg.

Arm title	12 to <17 Years Old IM Glucagon 1st Visit/NG 3.0 mg 2nd Visit

Arm description:

At the first visit, participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 Ibs, IM glucagon dose was 0.5 mg.

At the second visit, a NG dose of 3.0 mg was administered nasally.

Arm type	Active comparator
Investigational medicinal product name	Intramuscular Glucagon
Investigational medicinal product code	
Other name	Glucagon, GlucaGen HypoKit
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 lbs, IM glucagon dosed with 0.5 mg.

Investigational medicinal product name	Nasal Glucagon (NG)
Investigational medicinal product code	
Other name	Dry-Mist nasal glucagon, AMG504-1, LY900018
Pharmaceutical forms	Nasal powder
Routes of administration	Nasal use

Dosage and administration details:

NG doses of 3.0 mg for those 12 to less than 17 years of age were administered in a nostril with a prefilled delivery device that
delivered a single dose upon activation.

Number of subjects in period 1	4 to<8 Years Old Intramuscular (IM) Glucagon Visit	4 to <8 Years Old NG 2.0 mg 1st Visit/3.0 mg 2nd Visit	4 to <8 Years Old NG 3.0 mg 1st Visit/2.0 mg 2nd Visit
Started	6	6	6
Completed	6	6	6
Not completed	0	0	0
Consent withdrawn by subject	-	-	-

Number of subjects in period 1	8 to <12 Years Old Intramuscular Glucagon Visit	8 to <12 Years Old NG 2.0 mg 1st Visit/3.0 mg 2nd Visit	8 to <12 Years Old NG 3.0 mg 1st Visit/2.0 mg 2nd Visit
Started	6	6	6
Completed	6	6	5
Not completed	0	0	1
Consent withdrawn by subject	-	-	1

Number of subjects in period 1	12 to <17 Years Old NG 3.0 mg 1st Visit/IM Glucagon 2nd Visit	12 to <17 Years Old IM Glucagon 1st Visit/NG 3.0 mg 2nd Visit
Started	6	6
Completed	6	6
Not completed	0	0
Consent withdrawn by subject	-	-

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	48	48	
Age categorical Units: Subjects			
Age Continuous Units: years			
median	10.6		
inter-quartile range (Q1-Q3)	7.4 to 12.2	-	
Gender, Male/Female Units:			
Female	16	16	
Male	32	32	
Region of Enrollment Units: Subjects			
United States	48	48	
Duration of Diabetes Units: years			
median	3.9		
inter-quartile range (Q1-Q3)	2.6 to 6	-	
Local HbA1c (glycated haemoglobin) Units: Percentage			
arithmetic mean	8		
standard deviation	± 1	-	

Subject analysis sets

Subject analysis set title	4 to <8 Years Old IM Glucagon Cohort
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who were 4 to < 8 years old at the time of enrollment into the study randomized to receive only the intramuscular glucagon at one visit.

Subject analysis set title	4 to <8 Years Old NG Cohort
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who were 4 to < 8 years old at the time of enrollment into the study randomized to receive 2.0 or 3.0 mg of nasal glucagon at two separate visits. Order of these visits was randomized.

Subject analysis set title	8 to <12 Years Old IM Glucagon Cohort
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who were 8 to < 12 years old at the time of enrollment into the study randomized to receive only the intramuscular glucagon at one visit.

Subject analysis set title	8 to <12 Years Old NG Cohort

Subject analysis set type	Full analysis

Subject analysis set description:

Participants who were 8 to < 12 years old at the time of enrollment into the study randomized to receive 2.0 or 3.0 mg of nasal glucagon at two separate visits. Order of these visits was randomized.

Subject analysis set title	12 to <17 Years Old NG/IM Cohort
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who were 12 to < 17 years old at the time of enrollment into the study randomized to receive either intramuscular glucagon or nasal glucagon at two separate visits. Order of these visits was randomized.

Subject analysis set title	4 to<8 Years Old IM Glucagon Visit
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 Ibs, IM glucagon dose was 0.5 mg.

Subject analysis set title	4 to<8 Years Old NG Visit 2.0 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

NG dose of 2.0 mg for participants 4 to less than 8 years of age.

Subject analysis set title	4 to<8 Years Old NG Visit 3.0 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

NG dose of 3.0 mg for participants 4 to less than 8 years of age.

Subject analysis set title	8 to <12 Years Old IM Glucagon Visit
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 Ibs, IM glucagon dose was 0.5 mg.

Subject analysis set title	8 to<12 Years Old NG Visit 2.0 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

NG of 2.0 mg for participants 8 to less than 12 years of age.

Subject analysis set title	8 to<12 Years Old NG Visit 3.0 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

NG dose of 3.0 mg for participants 8 to less than 12 years of age.

Subject analysis set title	12 to <17 Years Old IM Glucagon Visit
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 Ibs, IM glucagon dose was 0.5 mg.

Subject analysis set title	12 to<17 Years Old NG Visit 3.0 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

NG dose of 3.0 mg for participants 12 to less than 17 years of age.

Reporting group values	4 to <8 Years Old IM Glucagon Cohort	4 to <8 Years Old NG Cohort	8 to <12 Years Old IM Glucagon Cohort
Number of subjects	6	12	6
Age categorical Units: Subjects			

Age Continuous Units: years median inter-quartile range (Q1-Q3)	 6.8 5.7 to 7.5	 6.8 5.7 to 7.5	 11.1 10.5 to 11.8
Gender, Male/Female Units:			
Female Male	0 6	3 9	3 3
Region of Enrollment Units: Subjects			
United States	6	12	6
Duration of Diabetes Units: years median inter-quartile range (Q1-Q3)	 3.1 2.1 to 3.8	 2.7 1.8 to 3.6	 5.3 3.9 to 6.3
Local HbA1c (glycated haemoglobin) Units: Percentage arithmetic mean standard deviation	 7.6 ± 0.5	 8.3 ± 0.8	 7.5 ± 1.1

Reporting group values	8 to <12 Years Old NG Cohort	12 to <17 Years Old NG/IM Cohort	4 to<8 Years Old IM Glucagon Visit
Number of subjects	12	12	6
Age categorical Units: Subjects			

Age Continuous Units: years median inter-quartile range (Q1-Q3)	 11.1 10.5 to 11.8	 14.5 13.2 to 15.8	
Gender, Male/Female Units:			
Female Male	5 7	5 7	
Region of Enrollment Units: Subjects			
United States	12	12	
Duration of Diabetes Units: years median inter-quartile range (Q1-Q3)	 4.3 3.4 to 6.7	 5.9 3.5 to 8.0	
Local HbA1c (glycated haemoglobin) Units: Percentage arithmetic mean standard deviation	 8.1 ± 0.7	 8.2 ± 1.5	 ±

Reporting group values	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg	8 to <12 Years Old IM Glucagon Visit
Number of subjects	12	12	6
Age categorical Units: Subjects			

Age Continuous Units: years median inter-quartile range (Q1-Q3)			
Gender, Male/Female Units:			
Female Male			
Region of Enrollment Units: Subjects			
United States			
Duration of Diabetes Units: years median inter-quartile range (Q1-Q3)			
Local HbA1c (glycated haemoglobin) Units: Percentage arithmetic mean standard deviation	±	±	±

Reporting group values	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg	12 to <17 Years Old IM Glucagon Visit
Number of subjects	11	12	12
Age categorical Units: Subjects			

Age Continuous Units: years median inter-quartile range (Q1-Q3)			
Gender, Male/Female Units:			
Female Male			
Region of Enrollment Units: Subjects			
United States			
Duration of Diabetes Units: years median inter-quartile range (Q1-Q3)			
Local HbA1c (glycated haemoglobin) Units: Percentage arithmetic mean standard deviation	±	±	±

Reporting group values	12 to<17 Years Old NG Visit 3.0 mg		
Number of subjects	12		
Age categorical Units: Subjects			

Age Continuous Units: years median inter-quartile range (Q1-Q3)			
Gender, Male/Female Units:			
Female Male			
Region of Enrollment Units: Subjects			
United States			
Duration of Diabetes Units: years median inter-quartile range (Q1-Q3)			
Local HbA1c (glycated haemoglobin) Units: Percentage arithmetic mean standard deviation	±		

End points

End points reporting groups

Reporting group title	4 to<8 Years Old Intramuscular (IM) Glucagon Visit
Reporting group description:	
This was completed at one visit and was the only visit for this cohort.	
Reporting group title	4 to <8 Years Old NG 2.0 mg 1st Visit/3.0 mg 2nd Visit
Reporting group description:	
At the first visit, a nasal glucagon (NG) dose of 2.0 milligrams (mg) for participants 4 to less than 8 years of age was administered nasally. At the second visit, NG dose of 3.0 mg was administered nasally.	
Reporting group title	4 to <8 Years Old NG 3.0 mg 1st Visit/2.0 mg 2nd Visit
Reporting group description:	
At the first visit, a NG dose of 3.0 mg for participants 4 to less than 8 years of age was administered nasally. At the second visit, a NG dose of 2.0 mg was administered nasally.	
Reporting group title	8 to <12 Years Old Intramuscular Glucagon Visit
Reporting group description:	
This was completed at one visit and was the only “dosing” visit for this cohort.	
Reporting group title	8 to <12 Years Old NG 2.0 mg 1st Visit/3.0 mg 2nd Visit
Reporting group description:	
At the first visit, a NG dose of 2.0 mg for participants 8 to less than 12 years of age was administered nasally. At the second visit, a NG dose of 3.0 mg was administered nasally.	
Reporting group title	8 to <12 Years Old NG 3.0 mg 1st Visit/2.0 mg 2nd Visit
Reporting group description:	
At the first visit, a NG dose of 3.0 mg for participants 8 to less than 12 years of age was administered nasally. At the second visit, a NG dose of 2.0 mg was administered nasally.	
Reporting group title	12 to <17 Years Old NG 3.0 mg 1st Visit/IM Glucagon 2nd Visit
Reporting group description:	
At the first visit, a NG dose of 3.0 mg was administered nasally. At the second visit, participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 Ibs, IM glucagon dose was 0.5 mg.	
Reporting group title	12 to <17 Years Old IM Glucagon 1st Visit/NG 3.0 mg 2nd Visit
Reporting group description:	
At the first visit, participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 Ibs, IM glucagon dose was 0.5 mg. At the second visit, a NG dose of 3.0 mg was administered nasally.	
Subject analysis set title	4 to <8 Years Old IM Glucagon Cohort
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who were 4 to < 8 years old at the time of enrollment into the study randomized to receive only the intramuscular glucagon at one visit.	
Subject analysis set title	4 to <8 Years Old NG Cohort
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who were 4 to < 8 years old at the time of enrollment into the study randomized to receive 2.0 or 3.0 mg of nasal glucagon at two separate visits. Order of these visits was randomized.	
Subject analysis set title	8 to <12 Years Old IM Glucagon Cohort

Subject analysis set type	Full analysis

Subject analysis set description:

Participants who were 8 to < 12 years old at the time of enrollment into the study randomized to receive only the intramuscular glucagon at one visit.

Subject analysis set title	8 to <12 Years Old NG Cohort
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who were 8 to < 12 years old at the time of enrollment into the study randomized to receive 2.0 or 3.0 mg of nasal glucagon at two separate visits. Order of these visits was randomized.

Subject analysis set title	12 to <17 Years Old NG/IM Cohort
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who were 12 to < 17 years old at the time of enrollment into the study randomized to receive either intramuscular glucagon or nasal glucagon at two separate visits. Order of these visits was randomized.

Subject analysis set title	4 to<8 Years Old IM Glucagon Visit
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 Ibs, IM glucagon dose was 0.5 mg.

Subject analysis set title	4 to<8 Years Old NG Visit 2.0 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

NG dose of 2.0 mg for participants 4 to less than 8 years of age.

Subject analysis set title	4 to<8 Years Old NG Visit 3.0 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

NG dose of 3.0 mg for participants 4 to less than 8 years of age.

Subject analysis set title	8 to <12 Years Old IM Glucagon Visit
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 Ibs, IM glucagon dose was 0.5 mg.

Subject analysis set title	8 to<12 Years Old NG Visit 2.0 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

NG of 2.0 mg for participants 8 to less than 12 years of age.

Subject analysis set title	8 to<12 Years Old NG Visit 3.0 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

NG dose of 3.0 mg for participants 8 to less than 12 years of age.

Subject analysis set title	12 to <17 Years Old IM Glucagon Visit
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who weighed at least 25 kg/55 lbs were dosed 1 mg of IM glucagon; participants who weighed less than 25 kg/55 Ibs, IM glucagon dose was 0.5 mg.

Subject analysis set title	12 to<17 Years Old NG Visit 3.0 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

NG dose of 3.0 mg for participants 12 to less than 17 years of age.

Primary: Maximum Change from Baseline Concentration (Cmax) of Glucagon

End point title	Maximum Change from Baseline Concentration (Cmax) of Glucagon[1]

End point description:

Change from baseline to maximum glucagon concentration within 90 minutes post glucagon administration.

Analysis Population Description: All enrolled participants that completed the required dosing visit(s). One participant in the 4 to <8 year old 2.0 mg NG group was excluded due to blowing nose after NG administration. One participant in the 8 to <12 group withdrew after completion of the 3.0 mg NG visit and did not complete the 2.0 mg NG visit.

End point type	Primary

End point timeframe:

Pre-dose; 5, 10, 15, 20, 30, 40, 60 and 90 minutes following glucagon administration.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Inferential statistics were exploratory only per protocol.

End point values	4 to<8 Years Old IM Glucagon Visit	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg	8 to <12 Years Old IM Glucagon Visit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	11	12	6
Units: picogram per milliliter (pg/mL)				
arithmetic mean (standard deviation)	6290.33 (± 2045.96)	3463.55 (± 1760.28)	3958.58 (± 2438.60)	4743.00 (± 3094.61)

End point values	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg	12 to <17 Years Old IM Glucagon Visit	12 to<17 Years Old NG Visit 3.0 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	12	12
Units: picogram per milliliter (pg/mL)				
arithmetic mean (standard deviation)	2776.27 (± 979.28)	5664.33 (± 2114.69)	4277.25 (± 3774.77)	3103.25 (± 2302.61)

Statistical analyses

No statistical analyses for this end point

Primary: Time to Maximum Concentration (Tmax) of Baseline Adjusted Glucagon

End point title	Time to Maximum Concentration (Tmax) of Baseline Adjusted Glucagon[2]

End point description:

Time to the change from baseline to maximum glucagon concentration within 90 minutes post glucagon administration.

Analysis Population Description: All enrolled participants that completed the required dosing visit(s). One participant in the 4 to <8 year old 2.0 mg NG group was excluded due to blowing nose after NG administration. One participant in the 8 to <12 group withdrew after completion of the 3.0 mg NG visit

and did not complete the 2.0 mg NG visit.

End point type	Primary

End point timeframe:

Pre-dose; 5, 10, 15, 20, 30, 40, 60 and 90 minutes following glucagon administration

Notes:

[2] - 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: Inferential statistical analyses were not performed

End point values	4 to<8 Years Old IM Glucagon Visit	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg	8 to <12 Years Old IM Glucagon Visit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	11	12	6
Units: hours				
median (full range (min-max))	0.29 (0.08 to 0.50)	0.25 (0.17 to 0.333)	0.29 (0.17 to 1.00)	0.29 (0.08 to 0.50)

End point values	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg	12 to <17 Years Old IM Glucagon Visit	12 to<17 Years Old NG Visit 3.0 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	12	12
Units: hours				
median (full range (min-max))	0.25 (0.17 to 0.33)	0.25 (0.17 to 0.50)	0.29 (0.08 to 0.50)	0.33 (0.25 to 0.50)

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Curve (AUC0-1.5) of Baseline Adjusted Glucagon

End point title	Area Under the Curve (AUC0-1.5) of Baseline Adjusted Glucagon[3]

End point description:

Area under the curve from pre-dose to the maximum change of glucagon concentration up to 90 minutes post glucagon administration.

Analysis Population Description: All enrolled participants that completed the required dosing visit(s). One participant in the 4 to <8 year old 2.0 mg NG group was excluded due to blowing nose after NG administration. One participant in the 8 to <12 group withdrew after completion of the 3.0 mg NG visit and did not complete the 2.0 mg NG visit.

End point type	Primary

End point timeframe:

Pre-dose; 5, 10, 15, 20, 30, 40, 60 and 90 minutes following glucagon administration

Notes:

[3] - 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: Inferential statistics were exploratory only per protocol.

End point values	4 to<8 Years Old IM Glucagon Visit	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg	8 to <12 Years Old IM Glucagon Visit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	11	12	6
Units: hour (hr).pg/mL				
arithmetic mean (standard deviation)	4078.68 (± 2078.89)	1744.36 (± 978.81)	2472.40 (± 1435.45)	3635.77 (± 2069.11)

End point values	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg	12 to <17 Years Old IM Glucagon Visit	12 to<17 Years Old NG Visit 3.0 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	12	12
Units: hour (hr).pg/mL				
arithmetic mean (standard deviation)	1506.23 (± 541.57)	2939.31 (± 1042.03)	3110.22 (± 2848.75)	1999.69 (± 1329.44)

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Concentration (Cmax) of Baseline-Adjusted Glucose

End point title	Maximum Concentration (Cmax) of Baseline-Adjusted

End point description:

The change from baseline to maximum glucose concentration within 90 minutes post glucagon administration.

Analysis Population Description: All enrolled participants that completed the required dosing visit(s). One participant in the 4 to <8 year old 2.0 mg NG group was excluded due to blowing nose after NG administration. One participant in the 8 to <12 group withdrew after completion of the 3.0 mg NG visit and did not complete the 2.0 mg NG visit.

End point type	Primary

End point timeframe:

Pre-dose; 5, 10, 15, 20, 30, 40, 60 and 90 minutes following glucagon administration.

Notes:

[4] - 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: Inferential statistics were exploratory only per protocol.

End point values	4 to<8 Years Old IM Glucagon Visit	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg	8 to <12 Years Old IM Glucagon Visit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	11	12	6
Units: mg/dL				
arithmetic mean (standard deviation)	138.17 (± 26.57)	118.18 (± 46.46)	137.50 (± 42.14)	130.50 (± 21.81)

End point values	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg	12 to <17 Years Old IM Glucagon Visit	12 to<17 Years Old NG Visit 3.0 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	12	12
Units: mg/dL				
arithmetic mean (standard deviation)	125.09 (± 23.81)	132.82 (± 30.59)	123.17 (± 29.58)	102.33 (± 25.63)

Statistical analyses

No statistical analyses for this end point

Primary: Time to Maximum Concentration (Tmax) of Baseline-Adjusted Glucose

End point title	Time to Maximum Concentration (Tmax) of Baseline-Adjusted Glucose[5]

End point description:

Time to the change from baseline to maximum glucose concentration within 90 minutest post glucagon administration.

Analysis Population Description: All enrolled participants that completed the required dosing visit(s). One participant in the 4 to <8 year old 2.0 mg NG group was excluded due to blowing nose after NG administration. One participant in the 8 to <12 group withdrew after completion of the 3.0 mg NG visit and did not complete the 2.0 mg NG visit.

End point type	Primary

End point timeframe:

Pre-dose; 5, 10, 15, 20, 30, 40, 60 and 90 minutes following glucagon administration.

Notes:

[5] - 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: Inferential statistical analyses were not performed

End point values	4 to<8 Years Old IM Glucagon Visit	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg	8 to <12 Years Old IM Glucagon Visit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	11	12	6
Units: hours				
median (full range (min-max))	1.00 (0.67 to 1.50)	0.67 (0.33 to 1.00)	1.00 (0.50 to 1.50)	1.50 (1.00 to 1.50)

End point values	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg	12 to <17 Years Old IM Glucagon Visit	12 to<17 Years Old NG Visit 3.0 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	12	12
Units: hours				

median (full range (min-max))	1.00 (0.67 to 1.50)	1.00 (0.50 to 1.50)	1.00 (0.67 to 1.50)	1.00 (0.50 to 1.50)

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Effect Concentration Time Curve (AUEC0-1.5) of Baseline-Adjusted Glucose From Time Zero up to 90 Minutes

End point title	Area Under the Effect Concentration Time Curve (AUEC0-1.5) of Baseline- Adjusted Glucose From Time Zero up to 90 Minutes[6]

End point description:

Area under the effect from pre-dose to the maximum change of glucose concentration up to 90 minutest post glucagon administration.

Analysis Population Description: All enrolled participants that completed the required dosing visit(s). One participant in the 4 to <8 year old 2.0 mg NG group was excluded due to blowing nose after NG administration. One participant in the 8 to <12 group withdrew after completion of the 3.0 mg NG visit and did not complete the 2.0 mg NG visit.

End point type	Primary

End point timeframe:

Pre-dose; 5, 10, 15, 20, 30, 40, 60 and 90 minutes following glucagon administration.

Notes:

[6] - 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: Inferential statistics were exploratory only per protocol.

End point values	4 to<8 Years Old IM Glucagon Visit	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg	8 to <12 Years Old IM Glucagon Visit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	11	12	6
Units: hr.mg/dL				
arithmetic mean (standard deviation)	145.86 (± 26.94)	118.82 (± 60.73)	142.38 (± 51.98)	132.42 (± 22.14)

End point values	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg	12 to <17 Years Old IM Glucagon Visit	12 to<17 Years Old NG Visit 3.0 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	12	12
Units: hr.mg/dL				
arithmetic mean (standard deviation)	128.82 (± 28.45)	138.12 (± 35.24)	126.94 (± 30.40)	101.46 (± 27.38)

Statistical analyses

No statistical analyses for this end point

Secondary: Nasal and Non-nasal Effects/Symptoms

End point title	Nasal and Non-nasal Effects/Symptoms

End point description:

Symptoms of runny nose, nasal congestion and/or itching, sneezing, watery and/or itchy eyes, redness of eyes, and itching of ears and/or throat were assessed prior to administering glucagon and at 15, 30, 60 and 90 minutes following administration of glucagon. This was done via the "Nasal Non-nasal Score Questionnaire". Each of the 9 symptoms is assigned an integer value from 0 to 3; higher values indicate more severe symptoms (a score of 0 indicates no symptoms). The reported results indicate the cohort median out of a possible maximum value of 27 (summing all 9 questions for each participant and reporting the median/IQR across participants).

End point type	Secondary

End point timeframe:

Pre-dose;15, 30, 60 and 90 minutes following glucagon administration.

Population: All enrolled participants. One participant in the 8 to <12 group withdrew from the study after completion of the 3.0 mg NG visit and did not complete the 2.0 mg NG visit.

End point values	4 to<8 Years Old IM Glucagon Visit	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg	8 to <12 Years Old IM Glucagon Visit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	12	12	6
Units: units on a scale				
median (inter-quartile range (Q1-Q3))				
Pre-dose	0.50 (0.00 to 1.00)	0.00 (0.00 to 2.00)	0.00 (0.00 to 1.00)	0.00 (0.00 to 0.00)
15 minutes post glucagon administration	0.00 (0.00 to 1.00)	1.00 (0.00 to 3.00)	0.50 (0.00 to 2.00)	0.00 (0.00 to 1.00)
30 minutes post glucagon administration	0.00 (0.00 to 1.00)	1.00 (0.00 to 1.50)	0.50 (0.00 to 1.50)	0.00 (0.00 to 1.00)
60 minutes post glucagon administration	0.00 (0.00 to 0.00)	0.50 (0.00 to 2.00)	0.00 (0.00 to 1.00)	0.00 (0.00 to 0.00)
90 minutes post glucagon administration	0.00 (0.00 to 0.00)	0.00 (0.00 to 1.50)	0.00 (0.00 to 0.50)	0.00 (0.00 to 0.00)

End point values	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg	12 to <17 Years Old IM Glucagon Visit	12 to<17 Years Old NG Visit 3.0 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	12	12
Units: units on a scale				
median (inter-quartile range (Q1-Q3))				
Pre-dose	0.00 (0.00 to 1.00)	0.00 (0.00 to 0.50)	0.00 (0.00 to 0.50)	0.50 (0.00 to 1.00)
15 minutes post glucagon administration	3.00 (0.00 to 4.00)	3.00 (1.00 to 4.50)	0.00 (0.00 to 0.00)	2.00 (1.00 to 4.00)
30 minutes post glucagon administration	2.00 (0.00 to 2.00)	2.50 (0.50 to 3.50)	0.00 (0.00 to 0.00)	1.00 (1.00 to 3.00)

60 minutes post glucagon administration	0.00 (0.00 to 1.00)	0.50 (0.00 to 1.50)	0.00 (0.00 to 0.00)	1.00 (0.00 to 2.00)
90 minutes post glucagon administration	0.00 (0.00 to 1.00)	0.00 (0.00 to 1.00)	0.00 (0.00 to 0.00)	1.00 (0.00 to 1.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Achieving at Least a 25 mg/dL Rise in Blood Glucose Above Nadir Level Within 30 Minutes

End point title	Number of Participants Achieving at Least a 25 mg/dL Rise in Blood Glucose Above Nadir Level Within 30 Minutes

End point description:

Glucose increase of at least 25 mg/dL above nadir within 30 Minutes following glucagon administration. Nadir is defined as the minimum glucose measurement at the time of or within 10 minutes following glucagon administration.

Analysis Population Description: All enrolled participants that completed the required dosing visit(s). One participant in the 4 to <8 year old 2.0 mg NG group was excluded due to blowing nose after NG administration. One participant in the 8 to <12 group withdrew after completion of the 3.0 mg NG visit and did not complete the 2.0 mg NG visit.

End point type	Secondary

End point timeframe:

Pre-dose; 5, 10, 15, 20, and 30 minutes following glucagon administration.

End point values	4 to<8 Years Old IM Glucagon Visit	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg	8 to <12 Years Old IM Glucagon Visit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	11	12	6
Units: Participants				
number (not applicable)	6	11	12	6

End point values	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg	12 to <17 Years Old IM Glucagon Visit	12 to<17 Years Old NG Visit 3.0 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	12	12
Units: Participants				
number (not applicable)	11	12	12	12

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Achieving ≥25 mg/dL Rise in Plasma Glucose Above Nadir Level Within 30 Minutes

End point title	Time to Achieving ≥25 mg/dL Rise in Plasma Glucose Above Nadir Level Within 30 Minutes

End point description:

Time (in minutes) when all participants experienced a rise in glucose >=25mg/dL.

Population Description: All enrolled participants that completed the required dosing visit(s). One participant in the 4 to <8 year old 2.0 mg NG group was excluded due to blowing nose after NG administration. One participant in the 8 to <12 group withdrew after completion of the 3.0 mg NG visit and did not complete the 2.0 mg NG visit.

End point type	Secondary

End point timeframe:

Pre-dose; 5, 10, 15, 20, and 30 minutes following glucagon administration.

End point values	4 to<8 Years Old IM Glucagon Visit	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg	8 to <12 Years Old IM Glucagon Visit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	11	12	6
Units: Minutes				
number (not applicable)	10	20	15	20

End point values	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg	12 to <17 Years Old IM Glucagon Visit	12 to<17 Years Old NG Visit 3.0 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	12	12
Units: Minutes				
number (not applicable)	20	15	20	20

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With >= 25 mg/dL Rise in Plasma Glucose Within 30 Minutes

End point title	Percentage of Participants With >= 25 mg/dL Rise in Plasma Glucose Within 30 Minutes

End point description:

Glucose increase of at least 25 mg/dL above nadir within 30 Minutes following glucagon administration. Nadir is defined as the minimum glucose measurement at the time of or within 10 minutes following glucagon administration.

Analysis Population Description: All enrolled participants that completed the required dosing visit(s). One participant in the 4 to <8 year old 2.0 mg NG group was excluded due to blowing nose after NG administration. One participant in the 8 to <12 group withdrew after completion of the 3.0 mg NG visit and did not complete the 2.0 mg NG visit.

End point type	Secondary

End point timeframe:

Pre-dose; 5, 10,15, 20, and 30 minutes following glucagon administration.

End point values	4 to<8 Years Old IM Glucagon Visit	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg	8 to <12 Years Old IM Glucagon Visit
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	11	12	6
Units: Percentage of participants				
number (not applicable)	100	100	100	100

End point values	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg	12 to <17 Years Old IM Glucagon Visit	12 to<17 Years Old NG Visit 3.0 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	11	12	12	12
Units: Percentage of participants				
number (not applicable)	100	100	100	100

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
Included all participants who received at least one dose of glucagon.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	4 to<8 Years Old IM Glucagon Visit
Reporting group description: -	
Reporting group title	4 to<8 Years Old NG Visit 2.0 mg
Reporting group description: -	
Reporting group title	4 to<8 Years Old NG Visit 3.0 mg
Reporting group description: -	
Reporting group title	8 to <12 Years Old IM Glucagon Visit
Reporting group description: -	
Reporting group title	8 to<12 Years Old NG Visit 2.0 mg
Reporting group description: -	
Reporting group title	8 to<12 Years Old NG Visit 3.0 mg
Reporting group description: -	
Reporting group title	12 to <17 Years Old IM Glucagon Visit
Reporting group description: -	
Reporting group title	12 to<17 Years Old NG Visit 3.0 mg
Reporting group description: -	

Serious adverse events	4 to<8 Years Old IM Glucagon Visit	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Endocrine disorders			
Hypoglycemia	Additional description: Experienced a hypoglycemic event after receiving a bolus of insulin with lunch. Received 90 grams oral carbohydrates and made a full recovery.		
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	8 to <12 Years Old IM Glucagon Visit	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg
Total subjects affected by serious			

adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Endocrine disorders			
Hypoglycemia	Additional description: Experienced a hypoglycemic event after receiving a bolus of insulin with lunch. Received 90 grams oral carbohydrates and made a full recovery.		
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	12 to <17 Years Old IM Glucagon Visit	12 to<17 Years Old NG Visit 3.0 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Endocrine disorders			
Hypoglycemia	Additional description: Experienced a hypoglycemic event after receiving a bolus of insulin with lunch. Received 90 grams oral carbohydrates and made a full recovery.		
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	4 to<8 Years Old IM Glucagon Visit	4 to<8 Years Old NG Visit 2.0 mg	4 to<8 Years Old NG Visit 3.0 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	6 / 12 (50.00%)	5 / 12 (41.67%)
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Catheter site pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Injection site discomfort			

subjects affected / exposed	2 / 6 (33.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lacrimation increase			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ocular discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Diarrhea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 6 (66.67%)	4 / 12 (33.33%)	2 / 12 (16.67%)
occurrences (all)	4	4	2
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	3 / 12 (25.00%)
occurrences (all)	1	1	3
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Sneezing			

subjects affected / exposed	0 / 6 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rhinalgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	1 / 12 (8.33%)
occurrences (all)	0	2	1

Non-serious adverse events	8 to <12 Years Old IM Glucagon Visit	8 to<12 Years Old NG Visit 2.0 mg	8 to<12 Years Old NG Visit 3.0 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	5 / 11 (45.45%)	6 / 12 (50.00%)
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Catheter site pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Injection site discomfort			
subjects affected / exposed	3 / 6 (50.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lacrimation increase			
subjects affected / exposed	0 / 6 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Ocular discomfort			

subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Diarrhea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	3 / 6 (50.00%)	1 / 11 (9.09%)	1 / 12 (8.33%)
occurrences (all)	3	1	1
Vomiting			
subjects affected / exposed	3 / 6 (50.00%)	3 / 11 (27.27%)	4 / 12 (33.33%)
occurrences (all)	3	3	4
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sneezing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rhinalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Headache			
subjects affected / exposed	2 / 6 (33.33%)	2 / 11 (18.18%)	4 / 12 (33.33%)
occurrences (all)	2	2	4

Non-serious adverse events	12 to <17 Years Old IM Glucagon Visit	12 to<17 Years Old NG Visit 3.0 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	9 / 12 (75.00%)	

Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Catheter site pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Injection site discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Lacrimation increase			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Ocular discomfort			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Diarrhea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	1 / 12 (8.33%)	3 / 12 (25.00%)	
occurrences (all)	1	2	
Vomiting			

subjects affected / exposed	5 / 12 (41.67%)	4 / 12 (33.33%)	
occurrences (all)	5	4	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Nasal discomfort			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Sneezing			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Rhinalgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Headache			
subjects affected / exposed	1 / 12 (8.33%)	4 / 12 (33.33%)	
occurrences (all)	1	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 October 2013	The protocol was modified to evaluate both doses (2.0 mg and 3.0 mg) in the age group of 4.0 to <12.0 years. Rather than having participants in this age group complete 3 research dosing visits (2.0 mg intranasal, 3.0 mg intranasal, and intramuscular). The sample size increased to 48 participants.
18 June 2014	The minimum weight requirement was removed from the protocol. Clarification was added that the number of blood draws will be reduced for participants who do not weigh enough to collect all blood samples for the study. The maximum amount of blood to be collected will remain at 5% of the participant's total blood volume.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported