



## Clinical trial results:

### Pen-Administered Low-Dose Dasiglucagon for Prevention and Treatment of Hypoglycemia in People with Type 1 Diabetes: A Randomized, Open-Label, Two-Period Crossover Outpatient Study

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2020-005745-16  |
| Trial protocol           | DK              |
| Global end of trial date | 28 January 2022 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 24 February 2023 |
| First version publication date | 24 February 2023 |

#### Trial information

##### Trial identification

|                       |       |
|-----------------------|-------|
| Sponsor protocol code | 77119 |
|-----------------------|-------|

##### Additional study identifiers

|                                    |  |
|------------------------------------|--|
| ISRCTN number                      | -  |
| ClinicalTrials.gov id (NCT number) | NCT04764968                                      |
| WHO universal trial number (UTN)   | -  |
| Other trial identifiers            | Regional Scientific Ethics Committee: H-21000002 |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Steno Diabetes Center Copenhagen  |
| Sponsor organisation address | Borgmester Ib Juuls Vej 83, Herlev, Denmark, 2730   |
| Public contact               | Christian Laugesen, Steno Diabetes Center Copenhagen, +45 51642387, christian.laugesen@regionh.dk |
| Scientific contact           | Christian Laugesen, Steno Diabetes Center Copenhagen, +45 51642387, christian.laugesen@regionh.dk |

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 14 November 2022 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 30 December 2021 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 28 January 2022  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the efficacy, safety and feasibility of outpatient-utilization of low-dose (80 µg) dasiglucagon administered via an investigational trial device (a multi-dose reusable pen injector) in preventing and treating mild hypoglycemia in insulin pump-treated people type 1 diabetes

Protection of trial subjects:

N/A

Background therapy:

All participants used their regular treatment modality (insulin pump therapy including stand-alone CGM).

Evidence for comparator:

N/A

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 27 April 2021 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Denmark: 24 |
| Worldwide total number of subjects   | 24          |
| EEA total number of subjects         | 24          |

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)                      | 20 |
| From 65 to 84 years                       | 4  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

Participants were recruited from the outpatient diabetes clinic at Steno Diabetes Center Copenhagen from May 2021 to November 2021.

### Pre-assignment

Screening details:

After providing oral and written informed consent, participants completed a screening visit for assessment of the eligibility criteria. Procedures included routine blood sampling, physical examination, review of medical history and medications as well as registration of baseline characteristics.

### Period 1

|                              |                               |
|------------------------------|-------------------------------|
| Period 1 title               | Study period (overall period) |
| Is this the baseline period? | Yes                           |
| Allocation method            | Randomised - controlled       |
| Blinding used                | Not blinded                   |

### Arms

|                              |                     |
|------------------------------|---------------------|
| Are arms mutually exclusive? | No                  |
| <b>Arm title</b>             | Dasiglucagon period |

Arm description:

2-week period where participants managed impending and manifested episodes of hypoglycaemia with pen-administered low-dose (80 µg) s.c. dasiglucagon using a multi-dose reusable pen injector.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | dasiglucagon   |
| Investigational medicinal product code |  |
| Other name                             | CAS15 number: 1544300-84-6, EV Substance code: SUB193123 |
| Pharmaceutical forms                   | Solution for injection                                   |
| Routes of administration               | Subcutaneous use   |

Dosage and administration details:

Administration of s.c. dasiglucagon (80 µg) using a multi-dose reusable pen injector.

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Usual care period |
|------------------|-------------------|

Arm description:

2-week period where participants managed impending and manifested episodes of hypoglycaemia with usual care (i.e. consumption of carbohydrates)

|   |            |
|---|------------|
| Arm type  | Usual care |
| No investigational medicinal product assigned in this arm |            |

| Number of subjects in period 1 | Dasiglucagon period | Usual care period |
|--------------------------------|---------------------|-------------------|
| Started                        | 24                  | 24                |
| Completed                      | 24                  | 24                |



## Baseline characteristics

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | Study period |
|-----------------------|--------------|

Reporting group description:

All 24 participants included in the study

| Reporting group values          | Study period | Total |  |
|---------------------------------|--------------|-------|--|
| Number of subjects              | 24           | 24    |  |
| Age categorical                 |              |       |  |
| Units: Subjects                 |              |       |  |
| Adults (18-64 years)            | 20           | 20    |  |
| From 65-84 years                | 4            | 4     |  |
| Age continuous                  |              |       |  |
| Units: years                    |              |       |  |
| arithmetic mean                 | 47           |       |  |
| standard deviation              | ± 15         | -     |  |
| Gender categorical              |              |       |  |
| Units: Subjects                 |              |       |  |
| Female                          | 14           | 14    |  |
| Male                            | 10           | 10    |  |
| Duration of diabetes            |              |       |  |
| Units: Years                    |              |       |  |
| arithmetic mean                 | 27           |       |  |
| standard deviation              | ± 13         | -     |  |
| Weight                          |              |       |  |
| Units: kilogram(s)              |              |       |  |
| arithmetic mean                 | 84.2         |       |  |
| standard deviation              | ± 14.2       | -     |  |
| Body mass index                 |              |       |  |
| Units: kilogram(s)/square metre |              |       |  |
| arithmetic mean                 | 28.3         |       |  |
| standard deviation              | ± 4.2        | -     |  |
| Systolic blood pressure         |              |       |  |
| Units: mmHg                     |              |       |  |
| arithmetic mean                 | 130          |       |  |
| standard deviation              | ± 15         | -     |  |
| Diastolic blood pressure        |              |       |  |
| Units: mmHg                     |              |       |  |
| arithmetic mean                 | 82           |       |  |
| standard deviation              | ± 7          | -     |  |
| Hemoglobin A1c                  |              |       |  |
| Units: mmol/mol                 |              |       |  |
| arithmetic mean                 | 56           |       |  |
| standard deviation              | ± 6          | -     |  |
| Hemoglobin A1c                  |              |       |  |
| Units: Percentage               |              |       |  |
| arithmetic mean                 | 7.3          |       |  |
| standard deviation              | ± 0.5        | -     |  |

|   |            |   |  |
|---|------------|---|--|
| Duration of insulin pump use<br>Units: Years<br>arithmetic mean<br>standard deviation | 8<br>± 1   | - |  |
| Total daily insulin dose<br>Units: Units<br>arithmetic mean<br>standard deviation     | 45<br>± 20 | - |  |
| Daily basal insulin dose<br>Units: Units<br>arithmetic mean<br>standard deviation     | 21<br>± 10 | - |  |
| Daily bolus insulin dose<br>Units: Units<br>arithmetic mean<br>standard deviation     | 24<br>± 11 | - |  |

### Subject analysis sets

|                            |                     |
|----------------------------|---------------------|
| Subject analysis set title | Dasiglucagon period |
| Subject analysis set type  | Full analysis       |

Subject analysis set description:

2-week period where participants managed impending and manifested episodes of hypoglycaemia with pen-administered low-dose (80 µg) s.c. dasiglucagon using a multi-dose reusable pen injector.

|                            |                   |
|----------------------------|-------------------|
| Subject analysis set title | Usual care period |
| Subject analysis set type  | Full analysis     |

Subject analysis set description:

2-week period where participants managed impending and manifested episodes of hypoglycaemia with usual care (i.e. consumption of carbohydrates)

| Reporting group values  | Dasiglucagon period | Usual care period |  |
|---|---------------------|-------------------|--|
| Number of subjects  | 24                  | 24                |  |
| Age categorical<br>Units: Subjects  |                     |                   |  |
| Adults (18-64 years)<br>From 65-84 years                                      |                     |                   |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation       | ±                   | ±                 |  |
| Gender categorical<br>Units: Subjects   |                     |                   |  |
| Female<br>Male  |                     |                   |  |
| Duration of diabetes<br>Units: Years<br>arithmetic mean<br>standard deviation | ±                   | ±                 |  |
| Weight<br>Units: kilogram(s)<br>arithmetic mean<br>standard deviation         | 84.2<br>± 14.2      | 84.2<br>± 14.2    |  |

|   |               |               |  |
|---|---------------|---------------|--|
| Body mass index<br>Units: kilogram(s)/square metre<br>arithmetic mean<br>standard deviation | 28.3<br>± 4.2 | 28.3<br>± 4.2 |  |
| Systolic blood pressure<br>Units: mmHg<br>arithmetic mean<br>standard deviation             | ±             | ±             |  |
| Diastolic blood pressure<br>Units: mmHg<br>arithmetic mean<br>standard deviation            | ±             | ±             |  |
| Hemoglobin A1c<br>Units: mmol/mol<br>arithmetic mean<br>standard deviation                  | ±             | ±             |  |
| Hemoglobin A1c<br>Units: Percentage<br>arithmetic mean<br>standard deviation                | 7.3<br>± 0.5  | 7.3<br>± 0.5  |  |
| Duration of insulin pump use<br>Units: Years<br>arithmetic mean<br>standard deviation       | ±             | ±             |  |
| Total daily insulin dose<br>Units: Units<br>arithmetic mean<br>standard deviation           | ±             | ±             |  |
| Daily basal insulin dose<br>Units: Units<br>arithmetic mean<br>standard deviation           | ±             | ±             |  |
| Daily bolus insulin dose<br>Units: Units<br>arithmetic mean<br>standard deviation           | ±             | ±             |  |



## End points

### End points reporting groups

|   |                     |
|---|---------------------|
| Reporting group title   | Dasiglucagon period |
| Reporting group description:<br>2-week period where participants managed impending and manifested episodes of hypoglycaemia with pen-administered low-dose (80 µg) s.c. dasiglucagon using a multi-dose reusable pen injector.      |                     |
| Reporting group title   | Usual care period   |
| Reporting group description:<br>2-week period where participants managed impending and manifested episodes of hypoglycaemia with usual care (i.e. consumption of carbohydrates)   |                     |
| Subject analysis set title  | Dasiglucagon period |
| Subject analysis set type   | Full analysis       |
| Subject analysis set description:<br>2-week period where participants managed impending and manifested episodes of hypoglycaemia with pen-administered low-dose (80 µg) s.c. dasiglucagon using a multi-dose reusable pen injector. |                     |
| Subject analysis set title  | Usual care period   |
| Subject analysis set type   | Full analysis       |
| Subject analysis set description:<br>2-week period where participants managed impending and manifested episodes of hypoglycaemia with usual care (i.e. consumption of carbohydrates)  |                     |

### Primary: Percentage of time in range (3.9-10 mmol/L)

|   |   |
|---|---|
| End point title   | Percentage of time in range (3.9-10 mmol/L) |
| End point description:  |   |
| End point type  | Primary                                     |
| End point timeframe:<br>2-week 'usual care' period and 2-week 'dasiglucagon' period |   |

| End point values                     | Dasiglucagon period  | Usual care period    |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 24                   | 24                   |  |  |
| Units: Percentage                    |                      |                      |  |  |
| arithmetic mean (standard deviation) | 63.5 (± 11)          | 61.1 (± 15)          |  |  |

### Statistical analyses

|   |   |
|---|---|
| Statistical analysis title  | Difference between interventions        |
| Statistical analysis description:<br>The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect. |   |
| Comparison groups   | Dasiglucagon period v Usual care period |

|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 48                             |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | other                          |
| P-value                                 | = 0.1286                       |
| Method                                  | Mixed models analysis          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | 2.4                            |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -0.7                           |
| upper limit                             | 5.5                            |

### Secondary: Percentage of time below range (<3.9 mmol/L)

|   |  |
|---|--|
| End point title   | Percentage of time below range (<3.9 mmol/L) |
| End point description:                                  |  |
| End point type  | Secondary                                    |
| End point timeframe:                                    |  |
| 2-week usual care period and 2-week dasiglucagon period |  |

| End point values                     | Dasiglucagon period  | Usual care period    |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 24                   | 24                   |  |  |
| Units: Percentage                    |                      |                      |  |  |
| arithmetic mean (standard deviation) | 2.5 (± 3)            | 3.1 (± 4)            |  |  |

### Statistical analyses

|  |   |
|--|---|
| Statistical analysis title   | Difference between interventions        |
| Statistical analysis description:  |   |
| The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect. |   |
| Comparison groups  | Dasiglucagon period v Usual care period |
| Number of subjects included in analysis  | 48                                      |
| Analysis specification   | Pre-specified                           |
| Analysis type  | other                                   |
| P-value  | = 0.1622                                |
| Method   | Mixed models analysis                   |
| Parameter estimate   | Mean difference (final values)          |
| Point estimate   | -0.5                                    |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -1.2    |
| upper limit         | 0.2     |

### Secondary: Percentage of time above range (>10 mmol/L)

|   |   |
|---|---|
| End point title   | Percentage of time above range (>10 mmol/L) |
| End point description:                                  |   |
| End point type  | Secondary                                   |
| End point timeframe:                                    |   |
| 2-week usual care period and 2-week dasiglucagon period |   |

| End point values                     | Dasiglucagon period  | Usual care period    |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 24                   | 24                   |  |  |
| Units: Percentage                    |                      |                      |  |  |
| arithmetic mean (standard deviation) | 33.9 (± 13)          | 35.8 (± 17)          |  |  |

### Statistical analyses

|  |   |
|--|---|
| Statistical analysis title   | Difference between interventions        |
| Statistical analysis description:  |   |
| The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect. |   |
| Comparison groups  | Dasiglucagon period v Usual care period |
| Number of subjects included in analysis  | 48                                      |
| Analysis specification   | Pre-specified                           |
| Analysis type  | other <sup>[1]</sup>                    |
| P-value  | = 0.2772                                |
| Method   | Mixed models analysis                   |
| Parameter estimate   | Mean difference (final values)          |
| Point estimate   | -1.9                                    |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -5.4                                    |
| upper limit  | 1.6                                     |

Notes:

[1] - The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect.

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**Secondary: Coefficient of variation**

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|                 |                          |
|-----------------|--------------------------|
| End point title | Coefficient of variation |
|-----------------|--------------------------|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

2-week usual care period and 2-week dasiglucagon period

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| End point values                     | Dasiglucagon period  | Usual care period    |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 24                   | 24                   |  |  |
| Units: Percentage                    |                      |                      |  |  |
| arithmetic mean (standard deviation) | 35.6 (± 4)           | 35.2 (± 5)           |  |  |

**Statistical analyses**

|                            |                                  |
|----------------------------|----------------------------------|
| Statistical analysis title | Difference between interventions |
|----------------------------|----------------------------------|

Statistical analysis description:

The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect.

|   |   |
|---|---|
| Comparison groups                       | Dasiglucagon period v Usual care period |
| Number of subjects included in analysis | 48                                      |
| Analysis specification                  | Pre-specified                           |
| Analysis type                           | other <sup>[2]</sup>                    |
| P-value                                 | = 0.5503                                |
| Method                                  | Mixed models analysis                   |
| Parameter estimate                      | Mean difference (final values)          |
| Point estimate                          | 0.4                                     |
| Confidence interval                     |   |
| level                                   | 95 %                                    |
| sides                                   | 2-sided                                 |
| lower limit                             | -1                                      |
| upper limit                             | 1.8                                     |

Notes:

[2] - The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect.

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**Secondary: Successful cases (%) of hypoglycemia treatment**

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|                 |  |
|-----------------|--|
| End point title | Successful cases (%) of hypoglycemia treatment |
|-----------------|--|

End point description:

Initial sensor glucose level  $\geq 2.2$  mmol/l and  $\leq 3.9$  mmol/l AND sensor glucose level  $> 3.9$  mmol/l 30 minutes post-treatment

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| 2-week 'usual care' period and 2-week 'dasiglucagon' period |           |

| End point values            | Dasiglucagon period  | Usual care period    |  |  |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type          | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed | 24                   | 24                   |  |  |
| Units: Percentage           |                      |                      |  |  |
| number (not applicable)     | 86                   | 77                   |  |  |

## Statistical analyses

|   |   |
|---|---|
| Statistical analysis title  | Difference between interventions        |
| Statistical analysis description:   |   |
| The endpoint was evaluated using a logistic regression model with random subject effect using sequence, period, and event baseline sensor glucose value as a covariate. |   |
| Comparison groups   | Dasiglucagon period v Usual care period |
| Number of subjects included in analysis   | 48                                      |
| Analysis specification  | Pre-specified                           |
| Analysis type   | other                                   |
| P-value   | = 0.1597                                |
| Method  | Regression, Logistic                    |
| Parameter estimate  | Odds ratio (OR)                         |
| Point estimate  | 1.55                                    |
| Confidence interval   |   |
| level   | 95 %                                    |
| sides   | 2-sided                                 |
| lower limit   | 0.84                                    |
| upper limit   | 2.86                                    |

## Secondary: Successful cases (%) of hypoglycemia treatment without subsequent hyperglycemia

|  |   |
|--|---|
| End point title  | Successful cases (%) of hypoglycemia treatment without subsequent hyperglycemia |
| End point description:   |   |
| Initial sensor glucose level $\geq 2.2$ mmol/l and $\leq 3.9$ mmol/l AND sensor glucose level $> 3.9$ mmol/l 30 minutes post-treatment AND sensor glucose level $\leq 10$ mmol/l during the first two hours post-treatment |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| 2-week 'usual care' period and 2-week 'dasiglucagon' period  |   |

| End point values            | Dasiglucagon period  | Usual care period    |  |  |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type          | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed | 24                   | 24                   |  |  |
| Units: Percentage           |                      |                      |  |  |
| number (not applicable)     | 57                   | 57                   |  |  |

## Statistical analyses

| Statistical analysis title  | Difference between interventions        |
|---|---|
| Statistical analysis description:   |   |
| The endpoint was evaluated using a logistic regression model with random subject effect using sequence, period, and event baseline sensor glucose value as a covariate. |   |
| Comparison groups   | Dasiglucagon period v Usual care period |
| Number of subjects included in analysis   | 48                                      |
| Analysis specification  | Pre-specified                           |
| Analysis type   | other                                   |
| P-value   | = 0.3215                                |
| Method  | Regression, Logistic                    |
| Parameter estimate  | Odds ratio (OR)                         |
| Point estimate  | 0.79                                    |
| Confidence interval   |   |
| level   | 95 %                                    |
| sides   | 2-sided                                 |
| lower limit   | 0.49                                    |
| upper limit   | 1.27                                    |

## Secondary: Successful cases (%) of hypoglycemia prevention

|   |   |
|---|---|
| End point title   | Successful cases (%) of hypoglycemia prevention |
| End point description:  |   |
| Initial sensor glucose level > 3.9 mmol/l AND sensor glucose level < 3.9 for ≤ 15 consecutive minutes during the first two hours post-treatment |   |
| End point type  | Secondary                                       |
| End point timeframe:  |   |
| 2-week 'usual care' period and 2-week 'dasiglucagon' period   |   |

| End point values            | Dasiglucagon period  | Usual care period    |  |  |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type          | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed | 24                   | 24                   |  |  |
| Units: Percentage           |                      |                      |  |  |
| number (not applicable)     | 90                   | 80                   |  |  |

## Statistical analyses

| Statistical analysis title   | Difference between interventions        |
|--|---|
| Statistical analysis description:<br>The endpoint was evaluated using a logistic regression model with random subject effect using sequence, period, and event baseline sensor glucose value as a covariate. |   |
| Comparison groups  | Dasiglucagon period v Usual care period |
| Number of subjects included in analysis  | 48                                      |
| Analysis specification   | Pre-specified                           |
| Analysis type  | other                                   |
| P-value  | = 0.0177                                |
| Method   | Regression, Logistic                    |
| Parameter estimate   | Odds ratio (OR)                         |
| Point estimate   | 3                                       |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | 1.21                                    |
| upper limit  | 7.41                                    |

## Secondary: Time (in minutes) from hypoglycemia treatment to euglycemia

|   |   |
|---|---|
| End point title   | Time (in minutes) from hypoglycemia treatment to euglycemia |
| End point description:<br>Minutes from initial sensor glucose level $\geq 2.2$ mmol/l and $\leq 3.9$ mmol/l to sensor glucose level $\geq 3.9$ mmol/l |   |
| End point type  | Secondary   |
| End point timeframe:<br>2-week 'usual care' period and 2-week 'dasiglucagon' period   |   |

| End point values                      | Dasiglucagon period  | Usual care period    |  |  |
|---------------------------------------|----------------------|----------------------|--|--|
| Subject group type                    | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed           | 24                   | 24                   |  |  |
| Units: Minutes                        |                      |                      |  |  |
| median (inter-quartile range (Q1-Q3)) | 16 (12 to 23)        | 21 (13 to 30)        |  |  |

## Statistical analyses

| Statistical analysis title   | Difference between interventions        |
|--|---|
| Statistical analysis description:<br>The endpoint was evaluated using a proportional hazards regression model with gamma-distributed random effect using sequence, period, and event baseline sensor glucose value as a covariate. |   |
| Comparison groups  | Dasiglucagon period v Usual care period |

|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 48              |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other           |
| P-value                                 | = 0.0064        |
| Method                                  | Regression, Cox |
| Parameter estimate                      | Rate ratio (RR) |
| Point estimate                          | 1.44            |
| Confidence interval                     |                 |
| level                                   | 95 %            |
| sides                                   | 2-sided         |
| lower limit                             | 1.11            |
| upper limit                             | 1.87            |

### Secondary: Incidence rate of supplement carbohydrate administration during the first hour following dasiglucagon administration

|                              |  |
|------------------------------|--|
| End point title              | Incidence rate of supplement carbohydrate administration during the first hour following dasiglucagon administration |
| End point description:       |  |
| End point type               | Secondary  |
| End point timeframe:         |  |
| 2-week 'dasiglucagon' period |  |

| End point values            | Dasiglucagon period  |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 24                   |  |  |  |
| Units: Number of episodes   | 22                   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Total daily insulin dose

|   |                          |
|---|--------------------------|
| End point title   | Total daily insulin dose |
| End point description:                                      |                          |
| End point type  | Secondary                |
| End point timeframe:  |                          |
| 2-week 'usual care' period and 2-week 'dasiglucagon' period |                          |



| End point values                     | Dasiglucagon period  | Usual care period    |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 24                   | 24                   |  |  |
| Units: Units                         |                      |                      |  |  |
| arithmetic mean (standard deviation) | 47.1 (± 22)          | 46.4 (± 20)          |  |  |

## Statistical analyses

| Statistical analysis title   | Difference between interventions        |
|--|---|
| Statistical analysis description:  |   |
| The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect. |   |
| Comparison groups  | Dasiglucagon period v Usual care period |
| Number of subjects included in analysis  | 48                                      |
| Analysis specification   | Pre-specified                           |
| Analysis type  | other                                   |
| P-value  | = 0.5148                                |
| Method   | Mixed models analysis                   |
| Parameter estimate   | Mean difference (final values)          |
| Point estimate   | 0.7                                     |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | -1.5                                    |
| upper limit  | 2.9                                     |

## Secondary: Total daily carbohydrate intake

|                              |                                 |
|------------------------------|---------------------------------|
| End point title              | Total daily carbohydrate intake |
| End point description:       |                                 |
| End point type               | Secondary                       |
| End point timeframe:         |                                 |
| 2-week 'dasiglucagon' period |                                 |

| End point values                     | Dasiglucagon period  | Usual care period    |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 24                   | 24                   |  |  |
| Units: grams                         |                      |                      |  |  |
| arithmetic mean (standard deviation) | 171 (± 59)           | 191 (± 66)           |  |  |

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Difference between interventions        |
| Statistical analysis description:<br>The treatment effect was evaluated by comparing treatment groups using a linear mixed model that included the factors treatment (2 levels), sequence (2 levels), period (2 levels), and a random subject effect. |   |
| Comparison groups   | Dasiglucagon period v Usual care period |
| Number of subjects included in analysis   | 48                                      |
| Analysis specification  | Pre-specified                           |
| Analysis type   | other                                   |
| P-value   | < 0.0001                                |
| Method  | Mixed models analysis                   |
| Parameter estimate  | Mean difference (final values)          |
| Point estimate  | -20                                     |
| Confidence interval   |   |
| level   | 95 %                                    |
| sides   | 2-sided                                 |
| lower limit   | -34                                     |
| upper limit   | -6                                      |

## Secondary: Patient-reported outcome

|  |                          |
|--|--------------------------|
| End point title  | Patient-reported outcome |
| End point description:<br>Percentage of participants scoring a favorable outcome on the patient-reported outcome questionnaire ("How likely is it that you, given the option, would use dasiglucagon as part of your diabetes management?" (Answer options: Very unlikely, unlikely, likely, very likely). |                          |
| End point type   | Secondary                |
| End point timeframe:<br>At the end-of-study visit  |                          |

|                             |                      |  |  |  |
|-----------------------------|----------------------|--|--|--|
| <b>End point values</b>     | Dasiglucagon period  |  |  |  |
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 24                   |  |  |  |
| Units: Percentage           |                      |  |  |  |
| number (not applicable)     | 96                   |  |  |  |

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

2-week 'usual care' period and 2-week 'dasiglucagon' period

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |     |
|-----------------|-----|
| Dictionary name | N/A |
|-----------------|-----|

|                    |     |
|--------------------|-----|
| Dictionary version | N/A |
|--------------------|-----|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Dasiglucagon period |
|-----------------------|---------------------|

Reporting group description: -

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Usual care period |
|-----------------------|-------------------|

Reporting group description: -

| Serious adverse events                            | Dasiglucagon period | Usual care period |  |
|---|---------------------|-------------------|--|
| Total subjects affected by serious adverse events |                     |                   |  |
| subjects affected / exposed                       | 0 / 24 (0.00%)      | 0 / 24 (0.00%)    |  |
| number of deaths (all causes)                     | 0                   | 0                 |  |
| number of deaths resulting from adverse events    | 0                   | 0                 |  |

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

| Non-serious adverse events                            | Dasiglucagon period | Usual care period |  |
|---|---------------------|-------------------|--|
| Total subjects affected by non-serious adverse events |                     |                   |  |
| subjects affected / exposed                           | 11 / 24 (45.83%)    | 10 / 24 (41.67%)  |  |
| Cardiac disorders                                     |                     |                   |  |
| Palpitations  |                     |                   |  |
| subjects affected / exposed                           | 3 / 24 (12.50%)     | 1 / 24 (4.17%)    |  |
| occurrences (all)                                     | 4                   | 1                 |  |
| Nervous system disorders                              |                     |                   |  |
| Headache  |                     |                   |  |
| subjects affected / exposed                           | 10 / 24 (41.67%)    | 8 / 24 (33.33%)   |  |
| occurrences (all)                                     | 36                  | 22                |  |
| Gastrointestinal disorders                            |                     |                   |  |
| Nausea  |                     |                   |  |
| subjects affected / exposed                           | 8 / 24 (33.33%)     | 4 / 24 (16.67%)   |  |
| occurrences (all)                                     | 34                  | 17                |  |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| Vomiting                    |                 |                 |  |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 24 (4.17%)  |  |
| occurrences (all)           | 0               | 1               |  |
| Stomachache                 |                 |                 |  |
| subjects affected / exposed | 4 / 24 (16.67%) | 3 / 24 (12.50%) |  |
| occurrences (all)           | 16              | 15              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported