



## Clinical trial results: Dasiglucagon in the treatment of postprandial hypoglycaemia after Roux-en-Y gastric bypass

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2019-001915-22   |
| Trial protocol           | DK               |
| Global end of trial date | 26 February 2020 |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 31 March 2021 |
| First version publication date | 31 March 2021 |

### Trial information

#### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | CKN-DASI-RYGB |
|-----------------------|---------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03984370 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Center for Clinical Metabolic Research at Gentofte Hospital   |
| Sponsor organisation address | Gentofte Hospitalsvej 7, hall 7, 3rd floor, Hellerup, Denmark, 2900   |
| Public contact               | Herlev-Gentofte Hospital, Center for Clinical Metabolic Research at Herlev-Gentofte Hospital, +45 60117434, casper.kjaersgaard.nielsen@regionh.dk |
| Scientific contact           | Herlev-Gentofte Hospital, Center for Clinical Metabolic Research at Herlev-Gentofte Hospital, +45 60117434, casper.kjaersgaard.nielsen@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                       | 26 February 2021 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 26 February 2020 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 26 February 2020 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

This was a proof-of-concept study aiming to evaluate the use of dasiglucagon in the management of postprandial hyperinsulinaemic hypoglycaemia in RYGB-operated individuals. To examine the effects of two different doses of dasiglucagon on the postprandial nadir plasma glucose concentration in RYGB-operated individuals suffering from postprandial hyperinsulinaemic hypoglycaemia by use of a mixed meal test (MMT).

The study was designed as a double-blinded, randomised, placebo-controlled, 3-period, 3-treatment, crossover study comprising 3 separate treatment days (MMTs).

Protection of trial subjects:

Participants are offered a healthy lunch followed by a 30-minute observation period after completion of each MMTs.

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 02 September 2019 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Denmark: 10 |
| Worldwide total number of subjects   | 10          |
| EEA total number of subjects         | 10          |

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)                      | 9 |

|                     |   |
|---------------------|---|
| From 65 to 84 years | 1 |
| 85 years and over   | 0 |

## Subject disposition

### Recruitment

Recruitment details:

- Oral and written information about the study.
- Oral and written informed consent.
- Review of inclusion and exclusion criteria.
- Measurement of blood pressure, pulse, weight and height.
- Fasting blood samples analysis including for, anaemia: basophilocytes, eosinophilocytes, erythrocytes, ferritin, haemoglobin, folate, iron, leukocytes, lymph

### Pre-assignment

Screening details:

A physician evaluated if inclusion criteria were fulfilled before enrollment

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | Overall (placebo, 80 and 200 ug dasiglu) (overall period) |
| Is this the baseline period? | Yes   |
| Allocation method            | Randomised - controlled                                   |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator                                     |

Blinding implementation details:

Blinding procedure was successful

### Arms

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

Arm description: -

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

Dosage and administration details:

0,4 mL of placebo

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | 80 ug dasiglucagon |
|------------------|--------------------|

Arm description: -

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Dasiglucagon           |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

80 ug dasiglucagon s.c. in abdomen

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | 200 ug dasiglucagon |
|------------------|---------------------|

Arm description: -

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |                        |
|--|------------------------|
| Investigational medicinal product name | Dasiglucagon           |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

200 ug dasiglucagon s.c. in abdomen

| <b>Number of subjects in period 1</b> | Placebo | 80 ug dasiglucagon | 200 ug dasiglucagon |
|---------------------------------------|---------|--------------------|---------------------|
| Started                               | 10      | 10                 | 10                  |
| Completed                             | 10      | 10                 | 10                  |

## Baseline characteristics

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Overall (placebo, 80 and 200 ug dasiglu) |
|-----------------------|--|

Reporting group description:

10 subjects at the baseline

| Reporting group values                             | Overall (placebo, 80 and 200 ug dasiglu) | Total |  |
|--|--|-------|--|
| Number of subjects                                 | 10                                       | 10    |  |
| Age categorical                                    |  |       |  |
| Units: Subjects                                    |  |       |  |
| In utero   | 0  | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0  | 0     |  |
| Newborns (0-27 days)                               | 0  | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0  | 0     |  |
| Children (2-11 years)                              | 0  | 0     |  |
| Adolescents (12-17 years)                          | 0  | 0     |  |
| Adults (18-64 years)                               | 9  | 9     |  |
| From 65-84 years                                   | 1  | 1     |  |
| 85 years and over                                  | 0  | 0     |  |
| Gender categorical                                 |  |       |  |
| Units: Subjects                                    |  |       |  |
| Female   | 8  | 8     |  |
| Male   | 2  | 2     |  |

## End points

### End points reporting groups

|                                |                     |
|--------------------------------|---------------------|
| Reporting group title          | Placebo             |
| Reporting group description: - |                     |
| Reporting group title          | 80 ug dasiglucagon  |
| Reporting group description: - |                     |
| Reporting group title          | 200 ug dasiglucagon |
| Reporting group description: - |                     |

### Primary: Nadir plasma glucose concentration

|  |                                    |
|--|------------------------------------|
| End point title  | Nadir plasma glucose concentration |
| End point description:   |                                    |
|  |                                    |
| End point type   | Primary                            |
| End point timeframe:   |                                    |
| Nadir plasma glucose concentration within 240 minutes after MMT. |                                    |

| End point values                 | Placebo           | 80 ug dasiglucagon | 200 ug dasiglucagon |  |
|----------------------------------|-------------------|--------------------|---------------------|--|
| Subject group type               | Reporting group   | Reporting group    | Reporting group     |  |
| Number of subjects analysed      | 10 <sup>[1]</sup> | 10 <sup>[2]</sup>  | 10 <sup>[3]</sup>   |  |
| Units: mmol/l                    |                   |                    |                     |  |
| arithmetic mean (standard error) | 3.0 (± 0.2)       | 3.9 (± 0.3)        | 4.5 (± 0.3)         |  |

Notes:

[1] - placebo

[2] - 80 ug

[3] - 200 ug

|                            |                                       |
|----------------------------|---------------------------------------|
| Attachments (see zip file) | Nadir glucose concentration/Nadir.pdf |
|----------------------------|---------------------------------------|

### Statistical analyses

|   |                                |
|---|--------------------------------|
| Statistical analysis title                                    | Pla vs. 200 ug                 |
| Statistical analysis description:                             |                                |
| A mixed model with Sidak corrections for multiple comparisons |                                |
| Comparison groups   | Placebo v 200 ug dasiglucagon  |
| Number of subjects included in analysis                       | 20                             |
| Analysis specification  | Post-hoc                       |
| Analysis type   |                                |
| P-value   | < 0.001                        |
| Method  | ANOVA                          |
| Parameter estimate  | Mean difference (final values) |
| Point estimate  | 1.4                            |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.81    |
| upper limit         | 2.05    |

|                                   |               |
|-----------------------------------|---------------|
| <b>Statistical analysis title</b> | Pla vs. 80 ug |
|-----------------------------------|---------------|

Statistical analysis description:

A mixed model with Sidak corrections for multiple comparisons

|   |                                |
|---|--------------------------------|
| Comparison groups                       | Placebo v 80 ug dasiglucagon   |
| Number of subjects included in analysis | 20                             |
| Analysis specification                  | Post-hoc                       |
| Analysis type                           | other                          |
| P-value                                 | < 0.01 <sup>[4]</sup>          |
| Method                                  | ANOVA                          |
| Parameter estimate                      | Mean difference (final values) |
| Point estimate                          | 0.9                            |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.35    |
| upper limit         | 1.35    |

Notes:

[4] - Sidak corrected



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

0-240 during the MMts

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |    |
|--------------------|----|
| Dictionary version | 23 |
|--------------------|----|

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | All adverse events |
|-----------------------|--------------------|

Reporting group description: -

| <b>Serious adverse events</b>                     | All adverse events |  |  |
|---|--------------------|--|--|
| Total subjects affected by serious adverse events |                    |  |  |
| subjects affected / exposed                       | 0 / 10 (0.00%)     |  |  |
| number of deaths (all causes)                     | 0                  |  |  |
| number of deaths resulting from adverse events    | 0                  |  |  |

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

| <b>Non-serious adverse events</b>                     | All adverse events |  |  |
|---|--------------------|--|--|
| Total subjects affected by non-serious adverse events |                    |  |  |
| subjects affected / exposed                           | 4 / 10 (40.00%)    |  |  |
| Gastrointestinal disorders                            |                    |  |  |
| Nausea  |                    |  |  |
| subjects affected / exposed                           | 3 / 10 (30.00%)    |  |  |
| occurrences (all)                                     | 3                  |  |  |
| Headache  |                    |  |  |
| subjects affected / exposed                           | 2 / 10 (20.00%)    |  |  |
| occurrences (all)                                     | 2                  |  |  |
| Abdominal pain  |                    |  |  |
| subjects affected / exposed                           | 1 / 10 (10.00%)    |  |  |
| occurrences (all)                                     | 1                  |  |  |
| Vomiting  |                    |  |  |
| subjects affected / exposed                           | 2 / 10 (20.00%)    |  |  |
| occurrences (all)                                     | 2                  |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| Dizziness                   |                 |  |  |
| subjects affected / exposed | 1 / 10 (10.00%) |  |  |
| occurrences (all)           | 1               |  |  |
| Sweatiness                  |                 |  |  |
| subjects affected / exposed | 1 / 10 (10.00%) |  |  |
| occurrences (all)           | 1               |  |  |

## 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