



## Clinical trial results:

### Effect and safety of semaglutide 2.4 mg once-weekly in subjects with overweight or obesity and type 2 diabetes

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-003414-10 |
| Trial protocol           | GB DE ES GR    |
| Global end of trial date | 01 May 2020    |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v2 (current) |
| This version publication date  | 02 July 2021 |
| First version publication date | 15 May 2021  |
| Version creation reason        |              |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | NN9536-4374 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |                  |
|------------------------------------|------------------|
| ISRCTN number                      | -                |
| ClinicalTrials.gov id (NCT number) | NCT03552757      |
| WHO universal trial number (UTN)   | U1111-1200-8148  |
| Other trial identifiers            | JapicCTI: 183992 |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Novo Nordisk A/S   |
| Sponsor organisation address | Novo Allé, Bagsværd, Denmark, 2880   |
| Public contact               | Clinical Transparency Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com |
| Scientific contact           | Clinical Transparency Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |                |
|--|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 28 August 2020 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 24 March 2020  |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 01 May 2020    |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

To compare the effect of semaglutide subcutaneous (s.c.; under the skin) 2.4 milligram (mg) once-weekly versus semaglutide placebo I/II as an adjunct to a reduced-calorie diet and increased physical activity in subjects with overweight or obesity and type 2 diabetes (T2D) on body weight.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013) and International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (2016) and 21 United States (US) Code of Federal Regulations (CFR) 312.120.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 04 June 2018 |
| 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 Arab Emirates: 38 |
| Country: Number of subjects enrolled | Argentina: 62            |
| Country: Number of subjects enrolled | Canada: 55               |
| Country: Number of subjects enrolled | Germany: 70              |
| Country: Number of subjects enrolled | Spain: 56                |
| Country: Number of subjects enrolled | United Kingdom: 86       |
| Country: Number of subjects enrolled | Greece: 47               |
| Country: Number of subjects enrolled | India: 164               |
| Country: Number of subjects enrolled | Japan: 125               |
| Country: Number of subjects enrolled | Russian Federation: 96   |
| Country: Number of subjects enrolled | United States: 361       |
| Country: Number of subjects enrolled | South Africa: 50         |
| Worldwide total number of subjects   | 1210                     |
| EEA total number of subjects         | 173                      |

Notes:

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**Subjects enrolled per age group**

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|   |     |
|---|-----|
| 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)                      | 953 |
| From 65 to 84 years                       | 257 |
| 85 years and over                         | 0   |

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## Subject disposition

### Recruitment

Recruitment details:

The trial was conducted at 149 sites in 12 countries as follows: Argentina (5 sites), Canada (10 sites), Germany (9 sites), Greece (6 sites), India (18 sites), Japan (12 sites), Russian Federation (9 sites), South Africa (6 sites), Spain (8 sites), United Arab Emirates (5 sites), United Kingdom (10 sites) and United States (51 sites).

### Pre-assignment

Screening details:

Subjects were randomised in 1:1:1 ratio to receive either 'semaglutide 2.4 milligram (mg) and placebo II (placebo matched to semaglutide 1.0 mg) once weekly', 'semaglutide 1.0 mg and placebo I (placebo matched to semaglutide 2.4 mg) once weekly' or 'placebo I and placebo II once weekly'.

### 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          |

Blinding implementation details:

Semaglutide and placebo were identical in appearance and were packed and labelled to fulfil the requirements for double-blind procedures.

### Arms

|                              |                    |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes                |
| <b>Arm title</b>             | Semaglutide 1.0 mg |

Arm description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8 and 1.0 mg from week 9-68. Subjects also received once-weekly placebo I (placebo matched to semaglutide 2.4 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

|  |                                 |
|--|---------------------------------|
| Arm type                               | Active comparator               |
| Investigational medicinal product name | Semaglutide B 1.34 mg/mL PDS290 |
| Investigational medicinal product code |                                 |
| Other name                             |                                 |
| Pharmaceutical forms                   | Solution for injection          |
| Routes of administration               | Subcutaneous use                |

Dosage and administration details:

Dosing was done once weekly with dose escalation every fourth week until semaglutide 1.0 mg was reached. Semaglutide was administered using a PDS290 pre-filled pen-injector containing semaglutide 1.34 mg/mL. Injection was done once weekly at the same day of the week (to the extent possible). Injections were administered in the thigh, abdomen or upper arm, and at any time of the day irrespective of meals.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Semaglutide 2.4 mg |
|------------------|--------------------|

Arm description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8, 1.0 mg from week 9-12, 1.7 mg from week 13-16 and 2.4 mg from week 17-68. Subjects also received once-weekly placebo II (placebo matched to semaglutide 1.0 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

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

|  |                                |
|--|--------------------------------|
| Investigational medicinal product name | Semaglutide B 1.0 mg/mL PDS290 |
| Investigational medicinal product code |                                |
| Other name                             |                                |
| Pharmaceutical forms                   | Solution for injection         |
| Routes of administration               | Subcutaneous use               |

Dosage and administration details:

Semaglutide 1.0 mg/mL was only dispensed at the first dispensing visit to cover the 0.25 and 0.5 mg dose escalation purposes. Semaglutide was administered using a PDS290 pre-filled pen-injector containing semaglutide 1.0 mg/mL. Injection was done once weekly at the same day of the week (to the extent possible). Injections were administered in the thigh, abdomen or upper arm, and at any time of the day irrespective of meals.

|  |                                |
|--|--------------------------------|
| Investigational medicinal product name | Semaglutide B 3.0 mg/mL PDS290 |
| Investigational medicinal product code |                                |
| Other name                             |                                |
| Pharmaceutical forms                   | Solution for injection         |
| Routes of administration               | Subcutaneous use               |

Dosage and administration details:

Dosing was done once weekly with dose escalation every fourth week until semaglutide 2.4 mg was reached. Semaglutide was administered using a PDS290 pre-filled pen-injector containing semaglutide 3.0 mg/mL. Injection was done once weekly at the same day of the week (to the extent possible). Injections were administered in the thigh, abdomen or upper arm, and at any time of the day irrespective of meals.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

Subjects received once-weekly s.c placebo injections (both placebo I (placebo matched to semaglutide 1.0 mg) and placebo II (placebo matched to semaglutide 2.4 mg) for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

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

Dosage and administration details:

Placebo I (placebo matched to semaglutide 2.4 mg) was administered using a PDS290 pre-filled pen-injector by subjects in both 'semaglutide 1.0 mg' and 'placebo' groups. Injection was done once weekly at the same day of the week (to the extent possible). Injections were administered in the thigh, abdomen or upper arm, and at any time of the day irrespective of meals.

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

Dosage and administration details:

Placebo II (placebo matched to semaglutide 1.0 mg) was administered using a PDS290 pre-filled pen-injector by subjects in both 'semaglutide 2.4 mg' and 'placebo' groups. Injection was done once weekly at the same day of the week (to the extent possible). Injections were administered in the thigh, abdomen or upper arm, and at any time of the day irrespective of meals.

| <b>Number of subjects in period 1</b> | Semaglutide 1.0 mg | Semaglutide 2.4 mg | Placebo |
|---------------------------------------|--------------------|--------------------|---------|
| Started                               | 403                | 404                | 403     |
| Exposed                               | 402                | 403                | 402     |
| Full analysis set (FAS)               | 403                | 404                | 403     |
| Safety analysis set (SAS)             | 402                | 403                | 402     |
| Completed                             | 390                | 391                | 383     |
| Not completed                         | 13                 | 13                 | 20      |
| Adverse event, serious fatal          | 1                  | 1                  | 1       |
| Consent withdrawn by subject          | 10                 | 5                  | 12      |
| Lost to follow-up                     | 2                  | 7                  | 7       |

## Baseline characteristics

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Semaglutide 1.0 mg |
|-----------------------|--------------------|

Reporting group description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8 and 1.0 mg from week 9-68. Subjects also received once-weekly placebo I (placebo matched to semaglutide 2.4 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Semaglutide 2.4 mg |
|-----------------------|--------------------|

Reporting group description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8, 1.0 mg from week 9-12, 1.7 mg from week 13-16 and 2.4 mg from week 17-68. Subjects also received once-weekly placebo II (placebo matched to semaglutide 1.0 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received once-weekly s.c placebo injections (both placebo I (placebo matched to semaglutide 1.0 mg) and placebo II (placebo matched to semaglutide 2.4 mg) for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

| Reporting group values | Semaglutide 1.0 mg | Semaglutide 2.4 mg | Placebo |
|------------------------|--------------------|--------------------|---------|
| Number of subjects     | 403                | 404                | 403     |
| Age Categorical        |                    |                    |         |
| Units: Subjects        |                    |                    |         |
| Adults (18-64 years)   | 320                | 316                | 317     |
| From 65-84 years       | 83                 | 88                 | 86      |
| Age Continuous         |                    |                    |         |
| Units: years           |                    |                    |         |
| arithmetic mean        | 56                 | 55                 | 55      |
| standard deviation     | ± 10               | ± 11               | ± 11    |
| Gender Categorical     |                    |                    |         |
| Units: Subjects        |                    |                    |         |
| Female                 | 203                | 223                | 190     |
| Male                   | 200                | 181                | 213     |

| Reporting group values | Total |  |  |
|------------------------|-------|--|--|
| Number of subjects     | 1210  |  |  |
| Age Categorical        |       |  |  |
| Units: Subjects        |       |  |  |
| Adults (18-64 years)   | 953   |  |  |
| From 65-84 years       | 257   |  |  |
| Age Continuous         |       |  |  |
| Units: years           |       |  |  |
| arithmetic mean        | -     |  |  |
| standard deviation     | -     |  |  |
| Gender Categorical     |       |  |  |
| Units: Subjects        |       |  |  |
| Female                 | 616   |  |  |
| Male                   | 594   |  |  |



## End points

### End points reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Semaglutide 1.0 mg |
|-----------------------|--------------------|

Reporting group description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8 and 1.0 mg from week 9-68. Subjects also received once-weekly placebo I (placebo matched to semaglutide 2.4 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Semaglutide 2.4 mg |
|-----------------------|--------------------|

Reporting group description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8, 1.0 mg from week 9-12, 1.7 mg from week 13-16 and 2.4 mg from week 17-68. Subjects also received once-weekly placebo II (placebo matched to semaglutide 1.0 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received once-weekly s.c placebo injections (both placebo I (placebo matched to semaglutide 1.0 mg) and placebo II (placebo matched to semaglutide 2.4 mg) for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

### Primary: Change in body weight (%) - semaglutide 2.4 mg versus placebo

|                 |  |
|-----------------|--|
| End point title | Change in body weight (%) - semaglutide 2.4 mg versus placebo <sup>[1]</sup> |
|-----------------|--|

End point description:

Change in body weight (%) from baseline (week 0) to week 68 is presented. Results are based on the data from both in-trial and on-treatment observation periods. In-trial observation period: the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact (week 75). On-treatment observation period: the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 2-week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least two consecutive missed doses. Number of subjects analysed = full analysis set (FAS) which comprised all randomised subjects. n = number of subjects with available data.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From baseline (week 0) to week 68

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

| End point values  | Semaglutide 2.4 mg | Placebo         |  |  |
|---|--------------------|-----------------|--|--|
| Subject group type  | Reporting group    | Reporting group |  |  |
| Number of subjects analysed   | 404                | 403             |  |  |
| Units: Percentage point of body weight arithmetic mean (standard deviation) |                    |                 |  |  |
| In-trial observation period (n=388 & 376)                                   | -9.9 (± 8.0)       | -3.3 (± 5.5)    |  |  |
| On-treatment observation period (n=351 & 340)                               | -10.7 (± 7.8)      | -3.1 (± 5.2)    |  |  |

## Statistical analyses

|   |                                   |
|---|-----------------------------------|
| <b>Statistical analysis title</b>   | Semaglutide 2.4 mg versus Placebo |
| Statistical analysis description:   |                                   |
| Results are based on the data from in-trial observation period. Week 68 responses were analysed using an analysis of covariance model (ANCOVA) with randomised treatment, stratification groups (oral anti-diabetic (OAD) treatment status and HbA1c category at screening) and the interaction between stratification groups as factors and baseline body weight as covariate. |                                   |
| Comparison groups   | Semaglutide 2.4 mg v Placebo      |
| Number of subjects included in analysis   | 807                               |
| Analysis specification  | Pre-specified                     |
| Analysis type   | superiority <sup>[2]</sup>        |
| P-value   | < 0.0001                          |
| Method  | ANCOVA                            |
| Parameter estimate  | Treatment difference              |
| Point estimate  | -6.21                             |
| Confidence interval   |                                   |
| level   | 95 %                              |
| sides   | 2-sided                           |
| lower limit   | -7.28                             |
| upper limit   | -5.15                             |

### Notes:

[2] - 'Number of subjects included in analysis' is being erroneously displayed as 807. It should be read as "number of subjects with an observation at week 68 = 764".

|  |                                   |
|--|-----------------------------------|
| <b>Statistical analysis title</b>  | Semaglutide 2.4 mg versus Placebo |
| Statistical analysis description:  |                                   |
| Results are based on the data from on-treatment observation period. All responses prior to first discontinuation of treatment (or initiation of other anti-obesity medication or bariatric surgery) were included in a mixed model for repeated measurements (MMRM) with randomised treatment, stratification groups (OAD treatment status and HbA1c category at screening) and the interaction between stratification groups as factors and baseline body weight as covariate, all nested within visit. |                                   |
| Comparison groups  | Semaglutide 2.4 mg v Placebo      |
| Number of subjects included in analysis  | 807                               |
| Analysis specification   | Pre-specified                     |
| Analysis type  | superiority <sup>[3]</sup>        |
| P-value  | < 0.0001                          |
| Method   | MMRM                              |
| Parameter estimate   | Treatment difference              |
| Point estimate   | -7.57                             |
| Confidence interval  |                                   |
| level  | 95 %                              |
| sides  | 2-sided                           |
| lower limit  | -8.56                             |
| upper limit  | -6.58                             |

Notes:

[3] - 'Number of subjects included in analysis' is being erroneously displayed as 807. It should be read as "number of subjects with an observation at week 68 = 633".

### Primary: Subjects who achieve body weight reduction $\geq 5\%$ from baseline (week 0) (yes/no) - semaglutide 2.4 mg versus placebo

|                 |  |
|-----------------|--|
| End point title | Subjects who achieve body weight reduction $\geq 5\%$ from baseline (week 0) (yes/no) - semaglutide 2.4 mg versus placebo <sup>[4]</sup> |
|-----------------|--|

End point description:

Number of subjects who achieved weight reduction  $\geq 5\%$  of their baseline body weight (yes/no) at week 68 is presented. Results are based on the data from both in-trial and on-treatment observation periods. In-trial observation period: the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. On-treatment observation period: the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 2 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least two consecutive missed doses. Number of subjects analysed = FAS which comprised all randomised subjects. n = number of subjects with available data.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

After 68 weeks

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

| End point values                                   | Semaglutide 2.4 mg | Placebo         |  |  |
|--|--------------------|-----------------|--|--|
| Subject group type                                 | Reporting group    | Reporting group |  |  |
| Number of subjects analysed                        | 404                | 403             |  |  |
| Units: Subjects                                    |                    |                 |  |  |
| In-trial observation period (n=388 & 376): Yes     | 267                | 107             |  |  |
| In-trial observation period (n=388 & 376): No      | 121                | 269             |  |  |
| On-treatment observation period (n=351 & 340): Yes | 257                | 94              |  |  |
| On-treatment observation period (n=351 & 340): No  | 94                 | 246             |  |  |

### Statistical analyses

|                            |                                   |
|----------------------------|-----------------------------------|
| Statistical analysis title | Semaglutide 2.4 mg versus Placebo |
|----------------------------|-----------------------------------|

Statistical analysis description:

Results are based on the data from in-trial observation period. Week 68 responses were analysed using a binary logistic regression model with randomised treatment, stratification groups (OAD treatment status and HbA1c category at screening) and the interaction between stratification groups as factors and baseline body weight as covariate.

|                   |                              |
|-------------------|------------------------------|
| Comparison groups | Semaglutide 2.4 mg v Placebo |
|-------------------|------------------------------|

|   |                            |
|---|----------------------------|
| Number of subjects included in analysis | 807                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | superiority <sup>[5]</sup> |
| P-value                                 | < 0.0001                   |
| Method                                  | Regression, Logistic       |
| Parameter estimate                      | Odds ratio (OR)            |
| Point estimate                          | 4.88                       |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 3.58                       |
| upper limit                             | 6.64                       |

Notes:

[5] - 'Number of subjects included in analysis' is being erroneously displayed as 807. It should be read as "number of subjects with an observation at week 68 = 764".

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Semaglutide 2.4 mg versus Placebo |
|-----------------------------------|-----------------------------------|

Statistical analysis description:

Results are based on the data from on-treatment observation period. All responses prior to first discontinuation of treatment (or initiation of other anti-obesity medication or bariatric surgery) were included in a MMRM with randomised treatment, stratification groups (OAD treatment status and HbA1c category at screening) and the interaction between stratification groups as factors and baseline body weight as covariate, all nested within visit.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Semaglutide 2.4 mg v Placebo |
| Number of subjects included in analysis | 807                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | superiority <sup>[6]</sup>   |
| P-value                                 | < 0.0001                     |
| Method                                  | Regression, Logistic         |
| Parameter estimate                      | Odds ratio (OR)              |
| Point estimate                          | 8.69                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 6.31                         |
| upper limit                             | 11.97                        |

Notes:

[6] - 'Number of subjects included in analysis' is being erroneously displayed as 807. It should be read as "number of subjects with an observation at week 68 = 633".

### **Secondary: Change in body weight (%) - semaglutide 2.4 mg versus semaglutide 1.0 mg**

|                 |   |
|-----------------|---|
| End point title | Change in body weight (%) - semaglutide 2.4 mg versus semaglutide 1.0 mg <sup>[7]</sup> |
|-----------------|---|

End point description:

Change in body weight (%) from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

From baseline (week 0) to week 68

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

| <b>End point values</b>                | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg |  |  |
|--|-----------------------|-----------------------|--|--|
| Subject group type                     | Reporting group       | Reporting group       |  |  |
| Number of subjects analysed            | 380                   | 388                   |  |  |
| Units: Percentage point of body weight |                       |                       |  |  |
| arithmetic mean (standard deviation)   | -7.2 (± 6.6)          | -9.9 (± 8.0)          |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Subjects who achieve (yes/no): Body weight reduction ≥10% from baseline (week 0)

|                 |  |
|-----------------|--|
| End point title | Subjects who achieve (yes/no): Body weight reduction ≥10% from baseline (week 0) |
|-----------------|--|

End point description:

Number of subjects who achieved weight reduction ≥10% of their baseline body weight (yes/no) at week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

After 68 weeks

| <b>End point values</b>     | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|-----------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type          | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed | 380                   | 388                   | 376             |  |
| Units: Subjects             |                       |                       |                 |  |
| Yes                         | 109                   | 177                   | 31              |  |
| No                          | 271                   | 211                   | 345             |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Subjects who achieve (yes/no): Body weight reduction ≥15% from baseline (week 0)

|                 |  |
|-----------------|--|
| End point title | Subjects who achieve (yes/no): Body weight reduction ≥15% from baseline (week 0) |
|-----------------|--|

End point description:

Number of subjects who achieved weight reduction  $\geq 15\%$  of their baseline body weight (yes/no) at week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type Secondary

End point timeframe:

After 68 weeks

| End point values            | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|-----------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type          | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed | 380                   | 388                   | 376             |  |
| Units: Subjects             |                       |                       |                 |  |
| Yes                         | 52                    | 100                   | 12              |  |
| No                          | 328                   | 288                   | 364             |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in waist circumference (cm)

End point title Change in waist circumference (cm)

End point description:

Change in waist circumference from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type Secondary

End point timeframe:

From baseline (week 0) to week 68

| End point values                     | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo           |  |
|--------------------------------------|-----------------------|-----------------------|-------------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group   |  |
| Number of subjects analysed          | 380                   | 387                   | 375               |  |
| Units: Centimetre (cm)               |                       |                       |                   |  |
| arithmetic mean (standard deviation) | -6.9 ( $\pm$ 6.8)     | -9.7 ( $\pm$ 8.1)     | -4.3 ( $\pm$ 6.5) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change in HbA1c (%)

End point title Change in HbA1c (%)

End point description:

Change in glycated haemoglobin (HbA1c (%)) from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type Secondary

End point timeframe:

From baseline (week 0) to week 68

| End point values                     | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|--------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed          | 376                   | 381                   | 374             |  |
| Units: Percentage point of HbA1c     |                       |                       |                 |  |
| arithmetic mean (standard deviation) | -1.5 (± 1.1)          | -1.7 (± 1.2)          | -0.3 (± 1.3)    |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in HbA1c (mmol/mol)

End point title Change in HbA1c (mmol/mol)

End point description:

Change in HbA1c (mmol/mol) from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type Secondary

End point timeframe:

From baseline (week 0) to week 68

| End point values                      | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|---------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                    | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed           | 376                   | 381                   | 374             |  |
| Units: millimoles per mole (mmol/mol) |                       |                       |                 |  |
| arithmetic mean (standard deviation)  | -16.9 (± 12.3)        | -18.7 (± 13.0)        | -3.4 (± 14.3)   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change in Systolic blood pressure (mmHg)

End point title Change in Systolic blood pressure (mmHg)

End point description:

Change in systolic blood pressure from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type Secondary

End point timeframe:

From baseline (week 0) to week 68

| End point values                     | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|--------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed          | 379                   | 387                   | 376             |  |
| Units: Millimetre of mercury (mmHg)  |                       |                       |                 |  |
| arithmetic mean (standard deviation) | -3 ( $\pm$ 15)        | -4 ( $\pm$ 14)        | 0 ( $\pm$ 15)   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change in diastolic blood pressure (mmHg)

End point title Change in diastolic blood pressure (mmHg)

End point description:

Change in diastolic blood pressure from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type Secondary

End point timeframe:

From baseline (week 0) to week 68

| <b>End point values</b>              | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|--------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed          | 379                   | 387                   | 376             |  |
| Units: Millimetre of mercury (mmHg)  |                       |                       |                 |  |
| arithmetic mean (standard deviation) | -1 (± 9)              | -2 (± 9)              | -1 (± 9)        |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in body weight (kg)

|                 |                            |
|-----------------|----------------------------|
| End point title | Change in body weight (kg) |
|-----------------|----------------------------|

End point description:

Change in body weight (kg) from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

From baseline (week 0) to week 68

| <b>End point values</b>              | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|--------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed          | 380                   | 388                   | 376             |  |
| Units: Kilogram (kg)                 |                       |                       |                 |  |
| arithmetic mean (standard deviation) | -7.1 (± 6.7)          | -9.9 (± 8.5)          | -3.4 (± 6.2)    |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in BMI (kg/sqm)

|                 |                        |
|-----------------|------------------------|
| End point title | Change in BMI (kg/sqm) |
|-----------------|------------------------|

End point description:

Change in body mass index (BMI) from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

From baseline (week 0) to week 68

| <b>End point values</b>                                  | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|--|-----------------------|-----------------------|-----------------|--|
| Subject group type                                       | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed                              | 380                   | 388                   | 376             |  |
| Units: kilogram per square meter<br>(kg/m <sup>2</sup> ) |                       |                       |                 |  |
| arithmetic mean (standard deviation)                     | -2.6 (± 2.4)          | -3.6 (± 3.1)          | -1.2 (± 2.1)    |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in fasting plasma glucose (FPG) (mg/dL)

|   |  |
|---|--|
| End point title   | Change in fasting plasma glucose (FPG) (mg/dL) |
| End point description:  |  |
| Change in fasting plasma glucose (FPG) from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data. |  |
| End point type  | Secondary                                      |
| End point timeframe:  |  |
| From baseline (week 0) to week 68   |  |

| <b>End point values</b>                 | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|---|-----------------------|-----------------------|-----------------|--|
| Subject group type                      | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed             | 367                   | 375                   | 370             |  |
| Units: milligrams per deciliter (mg/dL) |                       |                       |                 |  |
| arithmetic mean (standard deviation)    | -36.5 (± 45.1)        | -37.9 (± 45.9)        | -2.3 (± 53.1)   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in fasting serum insulin (mIU/L)

|  |   |
|--|---|
| End point title  | Change in fasting serum insulin (mIU/L) |
| End point description:   |   |
| Change in fasting serum insulin from baseline (week 0) to week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data. |   |

|                                   |           |
|-----------------------------------|-----------|
| End point type                    | Secondary |
| End point timeframe:              |           |
| From baseline (week 0) to week 68 |           |

| <b>End point values</b>              | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|--------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed          | 352                   | 360                   | 351             |  |
| Units: Picomoles per litre (pmol/L)  |                       |                       |                 |  |
| arithmetic mean (standard deviation) | 0.94 (± 59.8)         | 0.90 (± 65.4)         | 0.93 (± 53.6)   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in total cholesterol (mg/dL)

|   |                                     |
|---|-------------------------------------|
| End point title   | Change in total cholesterol (mg/dL) |
| End point description:  |                                     |
| Change in total cholesterol (measured in milligram per decilitre (mg/dL)) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data. |                                     |
| End point type  | Secondary                           |
| End point timeframe:  |                                     |
| From baseline (week 0) to week 68   |                                     |

| <b>End point values</b>                             | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|---|-----------------------|-----------------------|-----------------|--|
| Subject group type                                  | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed                         | 372                   | 380                   | 373             |  |
| Units: Ratio of total cholesterol                   |                       |                       |                 |  |
| geometric mean (geometric coefficient of variation) | 0.97 (± 20.1)         | 0.99 (± 17.9)         | 1.00 (± 18.9)   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in high density lipoprotein (HDL) cholesterol (mg/dL)

|  |  |
|--|--|
| End point title  | Change in high density lipoprotein (HDL) cholesterol (mg/dL) |
| End point description:   |  |
| Change in high density lipoprotein (HDL; measured in mg/dL) from baseline (week 0) to week 68 is |  |

presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

|                                   |           |
|-----------------------------------|-----------|
| End point type                    | Secondary |
| End point timeframe:              |           |
| From baseline (week 0) to week 68 |           |

| <b>End point values</b>                             | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo            |  |
|---|-----------------------|-----------------------|--------------------|--|
| Subject group type                                  | Reporting group       | Reporting group       | Reporting group    |  |
| Number of subjects analysed                         | 372                   | 375                   | 369                |  |
| Units: Ratio of HDL cholesterol                     |                       |                       |                    |  |
| geometric mean (geometric coefficient of variation) | 1.06 ( $\pm$ 16.0)    | 1.07 ( $\pm$ 15.7)    | 1.04 ( $\pm$ 15.3) |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in low density lipoprotein (LDL) cholesterol (mg/dL)

|  |   |
|--|---|
| End point title  | Change in low density lipoprotein (LDL) cholesterol (mg/dL) |
| End point description:   |   |
| Change in low density lipoprotein (LDL; measured in mg/dL) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| From baseline (week 0) to week 68  |   |

| <b>End point values</b>                             | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo            |  |
|---|-----------------------|-----------------------|--------------------|--|
| Subject group type                                  | Reporting group       | Reporting group       | Reporting group    |  |
| Number of subjects analysed                         | 372                   | 380                   | 373                |  |
| Units: Ratio of LDL cholesterol                     |                       |                       |                    |  |
| geometric mean (geometric coefficient of variation) | 0.99 ( $\pm$ 37.5)    | 1.00 ( $\pm$ 30.9)    | 1.00 ( $\pm$ 28.9) |  |

### Statistical analyses

No statistical analyses for this end point

**Secondary: Change in very low density lipoprotein (VLDL) cholesterol (mg/dL)**

|                 |   |
|-----------------|---|
| End point title | Change in very low density lipoprotein (VLDL) cholesterol (mg/dL) |
|-----------------|---|

End point description:

Change in very low density lipoprotein (VLDL; measured in mg/dL) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

From baseline (week 0) to week 68

| End point values                                    | Semaglutide 1.0 mg | Semaglutide 2.4 mg | Placebo         |  |
|---|--------------------|--------------------|-----------------|--|
| Subject group type                                  | Reporting group    | Reporting group    | Reporting group |  |
| Number of subjects analysed                         | 372                | 380                | 373             |  |
| Units: Ratio of VLDL cholesterol                    |                    |                    |                 |  |
| geometric mean (geometric coefficient of variation) | 0.82 (± 42.1)      | 0.80 (± 42.0)      | 0.92 (± 40.5)   |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change in free fatty acids (FFA)**

|                 |                                  |
|-----------------|----------------------------------|
| End point title | Change in free fatty acids (FFA) |
|-----------------|----------------------------------|

End point description:

Change in free fatty acids (measured in mg/dL) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

From baseline (week 0) to week 68

| End point values                                    | Semaglutide 1.0 mg | Semaglutide 2.4 mg | Placebo         |  |
|---|--------------------|--------------------|-----------------|--|
| Subject group type                                  | Reporting group    | Reporting group    | Reporting group |  |
| Number of subjects analysed                         | 353                | 361                | 354             |  |
| Units: Ratio of free fatty acids                    |                    |                    |                 |  |
| geometric mean (geometric coefficient of variation) | 0.85 (± 61.4)      | 0.84 (± 68.7)      | 1.01 (± 62.3)   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change in triglycerides

End point title | Change in triglycerides

End point description:

Change in triglycerides (measured in mg/dL) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type | Secondary

End point timeframe:

From baseline (week 0) to week 68

| End point values                                    | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo            |  |
|---|-----------------------|-----------------------|--------------------|--|
| Subject group type                                  | Reporting group       | Reporting group       | Reporting group    |  |
| Number of subjects analysed                         | 372                   | 380                   | 373                |  |
| Units: Ratio of triglycerides                       |                       |                       |                    |  |
| geometric mean (geometric coefficient of variation) | 0.81 ( $\pm$ 44.5)    | 0.79 ( $\pm$ 43.8)    | 0.92 ( $\pm$ 44.5) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change in high sensitivity C-Reactive Protein (hsCRP) (mg/L)

End point title | Change in high sensitivity C-Reactive Protein (hsCRP) (mg/L)

End point description:

Change in high sensitivity C-reactive protein (hsCRP; measured in milligram per litre (mg/L)) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

End point type | Secondary

End point timeframe:

From baseline (week 0) to week 68

| <b>End point values</b>                             | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo            |  |
|---|-----------------------|-----------------------|--------------------|--|
| Subject group type                                  | Reporting group       | Reporting group       | Reporting group    |  |
| Number of subjects analysed                         | 372                   | 380                   | 373                |  |
| Units: Ratio of hsCRP                               |                       |                       |                    |  |
| geometric mean (geometric coefficient of variation) | 0.59 ( $\pm$ 115.7)   | 0.50 ( $\pm$ 125.7)   | 0.84 ( $\pm$ 90.9) |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Plasminogen Activator Inhibitor-1 (PAI-1) Activity (AU/mL)

|                 |  |
|-----------------|--|
| End point title | Plasminogen Activator Inhibitor-1 (PAI-1) Activity (AU/mL) |
|-----------------|--|

End point description:

Change in Plasminogen Activator Inhibitor-1 (PAI-1; measured in arbitrary units per millilitre (AU/mL)) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

From baseline (week 0) to week 68

| <b>End point values</b>                             | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo            |  |
|---|-----------------------|-----------------------|--------------------|--|
| Subject group type                                  | Reporting group       | Reporting group       | Reporting group    |  |
| Number of subjects analysed                         | 334                   | 353                   | 336                |  |
| Units: Ratio of PAI-1 activity                      |                       |                       |                    |  |
| geometric mean (geometric coefficient of variation) | 1.21 ( $\pm$ 73.7)    | 1.06 ( $\pm$ 80.8)    | 1.42 ( $\pm$ 68.9) |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in Short Form 36 v2.0 acute (SF-36) (physical functioning score)

|                 |   |
|-----------------|---|
| End point title | Change in Short Form 36 v2.0 acute (SF-36) (physical functioning score) |
|-----------------|---|

End point description:

SF-36 is a 36-item patient-reported survey of patient health that measures the subject's overall health-related quality of life (HRQoL). SF-36v2™ questionnaire measured 8 domains of functional health and well-being as well as 2 component summary scores (physical component summary and mental

component summary). This endpoint shows results for 'physical functioning domain'. The 0-100 scale scores from the SF-36 were converted to norm-based scores to enable a direct interpretation in relation to the distribution of the scores in the 2009 U.S. general population. In the metric of norm-based scores, 50 and 10 corresponds to the mean and standard deviation respectively. Change from week 0 in the domain scores were evaluated at week 68. A positive change score indicates an improvement since baseline. Results are based on the data from in-trial observation period. This endpoint was evaluated based on the FAS. Number of subjects analysed = number of subjects with available data.

|                              |           |
|------------------------------|-----------|
| End point type               | Secondary |
| End point timeframe:         |           |
| Baseline (week 0) to week 68 |           |

| End point values                     | Semaglutide 1.0 mg | Semaglutide 2.4 mg | Placebo         |  |
|--------------------------------------|--------------------|--------------------|-----------------|--|
| Subject group type                   | Reporting group    | Reporting group    | Reporting group |  |
| Number of subjects analysed          | 370                | 376                | 365             |  |
| Units: Score on a scale              |                    |                    |                 |  |
| arithmetic mean (standard deviation) | 2.1 (± 6.8)        | 2.8 (± 7.7)        | 0.8 (± 7.0)     |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in SF-36 (all scores except physical functioning)

|                 |  |
|-----------------|--|
| End point title | Change in SF-36 (all scores except physical functioning) |
|-----------------|--|

End point description:

SF-36 is a 36-item patient-reported survey of patient health that measures the subject's overall health-related quality of life (HRQoL). SF-36v2™ questionnaire measured 8 domains of functional health and well-being as well as 2 component summary scores (physical component summary & mental component summary). This endpoint shows results for all the domains, except physical functioning. The 0-100 scale scores from the SF-36 were converted to norm-based scores to enable a direct interpretation in relation to the distribution of the scores in the 2009 U.S. general population. In the metric of norm-based scores, 50 and 10 corresponds to the mean and standard deviation respectively. Change from week 0 in the domain scores and component summary scores were evaluated at week 68. A positive change score indicates an improvement since baseline. Results are based on data from in-trial observation period. Analysis population=FAS. No. of subjects analysed=No. of subjects with available data.

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

End point timeframe:

From baseline (week 0) to week 68

| End point values                     | Semaglutide 1.0 mg | Semaglutide 2.4 mg | Placebo         |  |
|--------------------------------------|--------------------|--------------------|-----------------|--|
| Subject group type                   | Reporting group    | Reporting group    | Reporting group |  |
| Number of subjects analysed          | 370                | 376                | 365             |  |
| Units: Score on a scale              |                    |                    |                 |  |
| arithmetic mean (standard deviation) |                    |                    |                 |  |
| Role-Physical                        | 0.6 (± 6.9)        | 0.8 (± 7.4)        | 0.0 (± 7.1)     |  |
| Bodily Pain                          | 0.4 (± 8.3)        | 0.3 (± 9.0)        | -0.4 (± 8.6)    |  |
| General Health                       | 1.7 (± 7.2)        | 2.2 (± 7.3)        | 0.6 (± 7.5)     |  |

|                            |              |              |              |  |
|----------------------------|--------------|--------------|--------------|--|
| Vitality                   | -0.1 (± 7.8) | 0.8 (± 7.9)  | -0.9 (± 7.9) |  |
| Social Functioning         | -0.3 (± 6.6) | 0.2 (± 6.6)  | -0.7 (± 7.4) |  |
| Role-Emotional             | -0.4 (± 7.3) | -0.4 (± 7.7) | -1.1 (± 7.8) |  |
| Mental Health              | -0.9 (± 7.5) | -0.4 (± 6.9) | -1.6 (± 7.5) |  |
| Physical component summary | 1.9 (± 6.4)  | 2.3 (± 7.2)  | 0.9 (± 6.6)  |  |
| Mental component summary   | -1.4 (± 7.4) | -0.9 (± 6.9) | -1.8 (± 7.6) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change in IWQOL-Lite for CT (physical function domain (5-items) score)

|                 |  |
|-----------------|--|
| End point title | Change in IWQOL-Lite for CT (physical function domain (5-items) score) |
|-----------------|--|

End point description:

The Impact of Weight on Quality of Life Clinical Trials Version (IWQOL-Lite-CT) is designed to assess the impact of changes in weight on patients' quality of life within the context of clinical trials. IWQOL-Lite-CT is a 20-item questionnaire-based instrument used to assess the impact of body weight changes on subject's overall health-related quality of life (HRQoL). All IWQOL-Lite-CT composite scores range from 0 to 100, with higher scores reflecting better levels of functioning. This endpoint shows results for 'physical function domain'. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

From baseline (week 0) to week 68

| End point values                     | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|--------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed          | 369                   | 376                   | 365             |  |
| Units: Score on a scale              |                       |                       |                 |  |
| arithmetic mean (standard deviation) | 8.5 (± 18.8)          | 11.4 (± 20.8)         | 4.9 (± 20.4)    |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change in IWQOL-Lite for CT (all scores except physical function)

|                 |   |
|-----------------|---|
| End point title | Change in IWQOL-Lite for CT (all scores except physical function) |
|-----------------|---|

End point description:

The Impact of Weight on Quality of Life Clinical Trials Version (IWQOL-Lite-CT) is designed to assess the impact of changes in weight on patients' quality of life within the context of clinical trials. IWQOL-Lite-CT is a 20-item questionnaire-based instrument used to assess the impact of body weight changes on subject's overall health-related quality of life (HRQoL). All IWQOL-Lite-CT composite scores range from 0 to 100, with higher scores reflecting better levels of functioning. This endpoint shows results for

'physical and psychosocial domains, and for total'. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

|                                   |           |
|-----------------------------------|-----------|
| End point type                    | Secondary |
| End point timeframe:              |           |
| From baseline (week 0) to week 68 |           |

| <b>End point values</b>              | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|--------------------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed          | 369                   | 376                   | 365             |  |
| Units: Score on a scale              |                       |                       |                 |  |
| arithmetic mean (standard deviation) |                       |                       |                 |  |
| Physical                             | 7.6 (± 18.0)          | 11.0 (± 19.6)         | 4.4 (± 19.1)    |  |
| Psychosocial                         | 8.6 (± 15.7)          | 9.6 (± 16.7)          | 5.6 (± 16.5)    |  |
| Total                                | 8.2 (± 14.8)          | 10.1 (± 15.9)         | 5.2 (± 15.5)    |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Subjects who achieve (yes/no): Responder definition value for SF-36 physical functioning score

|                 |  |
|-----------------|--|
| End point title | Subjects who achieve (yes/no): Responder definition value for SF-36 physical functioning score |
|-----------------|--|

End point description:

Number of subjects experiencing a meaningful within subject improvement in SF-36 Physical function after 68 weeks was determined by two thresholds. The default generic responder threshold of 4.3 is for general population. The threshold of 3.7 is for overweight/obese population in the study and calculated using patient global rating anchor questionnaires to reflect subjects' own perspective based on Food and Drug Administration (FDA) recommendations. In the reported data, number of subjects who have achieved an improvement in score  $\geq$  to threshold are inferred as "Yes" and who have not achieved an improvement in score  $\geq$  to threshold are inferred as "No". The endpoint was evaluated based on in-trial observation period which is the uninterrupted time interval from randomization (week 0) to last trial related subject-site contact. The endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| After 68 weeks       |           |

| <b>End point values</b>     | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|-----------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type          | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed | 370                   | 376                   | 365             |  |
| Units: Subjects             |                       |                       |                 |  |
| Yes (with threshold 4.3)    | 88                    | 111                   | 68              |  |
| No (with threshold 4.3)     | 282                   | 265                   | 297             |  |
| Yes (with threshold 3.7)    | 130                   | 158                   | 102             |  |
| No (with threshold 3.7)     | 240                   | 218                   | 263             |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Subjects who achieve (yes/no): Responder definition value for IWQOL-Lite for CT physical function domain (5-items) score

|                        |  |
|------------------------|--|
| End point title        | Subjects who achieve (yes/no): Responder definition value for IWQOL-Lite for CT physical function domain (5-items) score   |
| End point description: | Number of subjects experiencing a meaningful within subject improvement in IWQOL-Lite-CT physical function after 68 weeks was determined by two thresholds. The preliminary responder threshold 20 was based on earlier studies. The threshold of 14.6 is for the overweight/obese population in the study and calculated using patient global rating anchor questionnaires to reflect subjects' own perspective based on FDA recommendations. In the reported data, number of subjects who have achieved an improvement in score $\geq$ to threshold are inferred as "Yes" and who have not achieved an improvement in score $\geq$ to threshold are inferred as "No". The endpoint was evaluated based on in-trial observation period which was the uninterrupted time interval from randomization (week 0) to last trial related subject-site contact. The endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data. |
| End point type         | Secondary  |
| End point timeframe:   | After 68 weeks   |

| <b>End point values</b>     | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|-----------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type          | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed | 369                   | 376                   | 365             |  |
| Units: Subjects             |                       |                       |                 |  |
| number (not applicable)     |                       |                       |                 |  |
| Yes (with threshold 20)     | 107                   | 131                   | 83              |  |
| No (with threshold 20)      | 262                   | 245                   | 282             |  |
| Yes (with threshold 14.6)   | 144                   | 160                   | 113             |  |
| No (with threshold 14.6)    | 225                   | 216                   | 252             |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Subjects who achieve (yes/no): HbA1c <7.0% (53 mmol/mol)**

|                 |  |
|-----------------|--|
| End point title | Subjects who achieve (yes/no): HbA1c <7.0% (53 mmol/mol) |
|-----------------|--|

End point description:

Number of subjects who achieved HbA1c <7% (yes/no) at week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

After 68 weeks

| End point values            | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|-----------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type          | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed | 376                   | 381                   | 374             |  |
| Units: Subjects             |                       |                       |                 |  |
| number (not applicable)     |                       |                       |                 |  |
| Yes                         | 272                   | 299                   | 99              |  |
| No                          | 104                   | 82                    | 275             |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Subjects who achieve (yes/no): HbA1c ≤6.5% (48 mmol/mol)**

|                 |  |
|-----------------|--|
| End point title | Subjects who achieve (yes/no): HbA1c ≤6.5% (48 mmol/mol) |
|-----------------|--|

End point description:

Number of subjects who achieved HbA1c ≤6.5% (yes/no) at week 68 is presented. Results are based on the data from in-trial observation period which was defined as the uninterrupted time interval from the start of randomisation (week 0) to last trial-related subject-site contact. This endpoint was evaluated based on the FAS which comprised all randomised subjects. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

After 68 weeks

| End point values            | Semaglutide<br>1.0 mg | Semaglutide<br>2.4 mg | Placebo         |  |
|-----------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type          | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed | 376                   | 381                   | 374             |  |
| Units: Subjects             |                       |                       |                 |  |
| Yes                         | 226                   | 257                   | 58              |  |
| No                          | 150                   | 124                   | 316             |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of treatment-emergent adverse events (TEAEs) - semaglutide 2.4 mg versus placebo

|                 |  |
|-----------------|--|
| End point title | Number of treatment-emergent adverse events (TEAEs) - semaglutide 2.4 mg versus placebo <sup>[8]</sup> |
|-----------------|--|

End point description:

Adverse events (AEs) with onset during the on-treatment observation period were defined as treatment-emergent AEs (TEAEs). On-treatment observation period: the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 7 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least seven consecutive missed doses. This endpoint was evaluated based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

From baseline (week 0) to week 75

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

| End point values            | Semaglutide 2.4 mg | Placebo         |  |  |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type          | Reporting group    | Reporting group |  |  |
| Number of subjects analysed | 403                | 402             |  |  |
| Units: Events               | 2197               | 1388            |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of serious adverse events (SAEs) - semaglutide 2.4 mg versus placebo

|                 |  |
|-----------------|--|
| End point title | Number of serious adverse events (SAEs) - semaglutide 2.4 mg versus placebo <sup>[9]</sup> |
|-----------------|--|

End point description:

Serious adverse event (SAE) results are based on the on-treatment observation period, which was defined as the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 7 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least seven consecutive missed doses. This endpoint was evaluated based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

From baseline (week 0) to week 75

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

| <b>End point values</b>     | Semaglutide 2.4 mg | Placebo         |  |  |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type          | Reporting group    | Reporting group |  |  |
| Number of subjects analysed | 403                | 402             |  |  |
| Units: Events               | 71                 | 53              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of treatment emergent severe or blood glucose confirmed symptomatic hypoglycaemia episodes - semaglutide 2.4 mg versus placebo

|                 |   |
|-----------------|---|
| End point title | Number of treatment emergent severe or blood glucose confirmed symptomatic hypoglycaemia episodes - semaglutide 2.4 mg versus placebo <sup>[10]</sup> |
|-----------------|---|

End point description:

Hypoglycaemic episodes with onset during the on-treatment observation period were considered treatment-emergent. On-treatment observation period was defined as the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 7 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least 7 consecutive missed doses. Severe hypoglycaemia: An episode requiring assistance of another person to actively administer carbohydrate, glucagon or take other corrective actions. plasma glucose (PG) concentrations may not be available during an event, but neurological recovery following the return of PG to normal is considered sufficient evidence that the event was induced by a low PG concentration. Blood glucose (BG) confirmed symptomatic hypoglycaemia: An episode that is BG confirmed by PG value <3.1 mmol/L (56 mg/dL) with symptoms consistent with hypoglycaemia.

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

End point timeframe:

From baseline (week 0) to week 75

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

| <b>End point values</b>     | Semaglutide 2.4 mg | Placebo         |  |  |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type          | Reporting group    | Reporting group |  |  |
| Number of subjects analysed | 403                | 402             |  |  |
| Units: Episodes             | 51                 | 18              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change in pulse (bpm) - semaglutide 2.4 mg versus placebo

End point title | Change in pulse (bpm) - semaglutide 2.4 mg versus placebo<sup>[11]</sup>

End point description:

Change in pulse from baseline (week 0) to week 68 is presented. Results are based on the data from on-treatment observation period, which was defined as the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 2 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least two consecutive missed doses. This endpoint was evaluated based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment. Number of subjects analysed = number of subjects with available data.

End point type | Secondary

End point timeframe:

From baseline (week 0) to week 68

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

| End point values                     | Semaglutide 2.4 mg | Placebo         |  |  |
|--------------------------------------|--------------------|-----------------|--|--|
| Subject group type                   | Reporting group    | Reporting group |  |  |
| Number of subjects analysed          | 351                | 340             |  |  |
| Units: Beats/minute                  |                    |                 |  |  |
| arithmetic mean (standard deviation) | 2 (± 9)            | 0 (± 9)         |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in amylase (U/L) - semaglutide 2.4 mg versus placebo

End point title | Change in amylase (U/L) - semaglutide 2.4 mg versus

End point description:

Change in amylase (units/litre) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from on-treatment observation period, which was defined as the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 2 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least two consecutive missed doses. This endpoint was evaluated based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment. Number of subjects analysed = number of subjects with available data.

End point type | Secondary

End point timeframe:

From baseline (week 0) to week 68

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

| <b>End point values</b>                             | Semaglutide<br>2.4 mg | Placebo            |  |  |
|---|-----------------------|--------------------|--|--|
| Subject group type                                  | Reporting group       | Reporting group    |  |  |
| Number of subjects analysed                         | 350                   | 338                |  |  |
| Units: Ratio of amylase                             |                       |                    |  |  |
| geometric mean (geometric coefficient of variation) | 1.24 ( $\pm$ 28.3)    | 1.06 ( $\pm$ 25.0) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in lipase (U/L) - semaglutide 2.4 mg versus placebo

|                 |  |
|-----------------|--|
| End point title | Change in lipase (U/L) - semaglutide 2.4 mg versus placebo <sup>[13]</sup> |
|-----------------|--|

End point description:

Change in lipase (units/litre) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from on-treatment observation period, which was defined as the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 2 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least two consecutive missed doses. This endpoint was evaluated based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment. Number of subjects analysed = number of subjects with available data.

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

End point timeframe:

From baseline (week 0) to week 68

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

| <b>End point values</b>                             | Semaglutide<br>2.4 mg | Placebo            |  |  |
|---|-----------------------|--------------------|--|--|
| Subject group type                                  | Reporting group       | Reporting group    |  |  |
| Number of subjects analysed                         | 350                   | 338                |  |  |
| Units: Ratio of lipase                              |                       |                    |  |  |
| geometric mean (geometric coefficient of variation) | 1.41 ( $\pm$ 57.2)    | 0.99 ( $\pm$ 51.8) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in calcitonin - semaglutide 2.4 mg versus placebo

|                 |  |
|-----------------|--|
| End point title | Change in calcitonin - semaglutide 2.4 mg versus placebo <sup>[14]</sup> |
|-----------------|--|

End point description:

Change in calcitonin (nanogram/litre) from baseline (week 0) to week 68 is presented as ratio to baseline. Results are based on the data from on-treatment observation period, which was defined as the interval from the date of first trial product administration (week 0) to the date of last trial product administration (week 68) plus a 2 week follow-up period and excluding any off-treatment time intervals. Off-treatment time interval: time period with at least two consecutive missed doses. This endpoint was

evaluated based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment. Number of subjects analysed = number of subjects with available data.

---

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

---

End point timeframe:

From baseline (week 0) to week 68

---

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint compared 'Semaglutide 2.4 mg arm' with 'Placebo arm', thus values only for these two arms are provided.

| <b>End point values</b>                             | Semaglutide 2.4 mg | Placebo            |  |  |
|---|--------------------|--------------------|--|--|
| Subject group type                                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed                         | 348                | 339                |  |  |
| Units: Ratio of calcitonin                          |                    |                    |  |  |
| geometric mean (geometric coefficient of variation) | 0.94 ( $\pm$ 60.3) | 0.96 ( $\pm$ 38.6) |  |  |

## Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Week 0 to week 75. Results are based on the SAS which included all randomised subjects exposed to at least one dose of randomised treatment.

Adverse event reporting additional description:

All presented AEs are treatment-emergent (i.e., TEAEs).

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 22 |
|--------------------|----|

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Semaglutide 1.0 mg |
|-----------------------|--------------------|

Reporting group description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8 and 1.0 mg from week 9-68. Subjects also received once-weekly placebo I (placebo matched to semaglutide 2.4 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Semaglutide 2.4 mg |
|-----------------------|--------------------|

Reporting group description:

Subjects received once-weekly s.c semaglutide injections for 68 weeks: 0.25 mg from week 1-4, 0.5 mg from week 5-8, 1.0 mg from week 9-12, 1.7 mg from week 13-16 and 2.4 mg from week 17-68. Subjects also received once-weekly placebo II (placebo matched to semaglutide 1.0 mg) s.c. injection for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received once-weekly s.c placebo injections (both placebo I (placebo matched to semaglutide 1.0 mg) and placebo II (placebo matched to semaglutide 2.4 mg) for 68 weeks. Subjects received the treatments as an adjunct to a reduced calorie diet and increased physical activity.

| Serious adverse events  | Semaglutide 1.0 mg | Semaglutide 2.4 mg | Placebo          |
|---|--------------------|--------------------|------------------|
| Total subjects affected by serious adverse events                   |                    |                    |                  |
| subjects affected / exposed   | 31 / 402 (7.71%)   | 40 / 403 (9.93%)   | 37 / 402 (9.20%) |
| number of deaths (all causes)                                       | 0                  | 1                  | 1                |
| number of deaths resulting from adverse events                      | 0                  | 0                  | 0                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                    |                    |                  |
| Adenocarcinoma gastric  |                    |                    |                  |
| subjects affected / exposed   | 1 / 402 (0.25%)    | 0 / 403 (0.00%)    | 0 / 402 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 1              | 0 / 0              | 0 / 0            |
| deaths causally related to treatment / all                          | 0 / 0              | 0 / 0              | 0 / 0            |
| Adenocarcinoma of colon   |                    |                    |                  |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                         | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastric cancer                                      |                 |                 |                 |
| subjects affected / exposed                         | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all     | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastric cancer stage IV                             |                 |                 |                 |
| subjects affected / exposed                         | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all     | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal lymphoma                           |                 |                 |                 |
| subjects affected / exposed                         | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal stromal tumour                     |                 |                 |                 |
| subjects affected / exposed                         | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (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           |
| Hepatocellular carcinoma                            |                 |                 |                 |
| subjects affected / exposed                         | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all     | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           | 0 / 1           |
| Invasive ductal breast carcinoma                    |                 |                 |                 |
| subjects affected / exposed                         | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           | 0 / 0           |
| Keratinising squamous cell carcinoma of nasopharynx |                 |                 |                 |
| subjects affected / exposed                         | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all     | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all          | 0 / 0           | 0 / 0           | 0 / 0           |
| Myeloid leukaemia                                   |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Neuroendocrine tumour</b>                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Prostate cancer</b>                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 2 / 402 (0.50%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Uterine cancer</b>                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Vascular disorders</b>                       |                 |                 |                 |
| <b>Aortic rupture</b>                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Hypertension</b>                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 2 / 403 (0.50%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Hypertensive urgency</b>                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Shock</b>                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Surgical and medical procedures</b>          |                 |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| Cardiac pacemaker replacement<br>subjects affected / exposed | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to<br>treatment / all           | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to<br>treatment / all                | 0 / 0           | 0 / 0           | 0 / 0           |
| Sperm aspiration<br>subjects affected / exposed              | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to<br>treatment / all           | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to<br>treatment / all                | 0 / 0           | 0 / 0           | 0 / 0           |
| Stent placement<br>subjects affected / exposed               | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to<br>treatment / all           | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to<br>treatment / all                | 0 / 0           | 0 / 0           | 0 / 0           |
| Thyroidectomy<br>subjects affected / exposed                 | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to<br>treatment / all           | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to<br>treatment / all                | 0 / 0           | 0 / 0           | 0 / 0           |
| Pregnancy, puerperium and perinatal<br>conditions            |                 |                 |                 |
| Abortion spontaneous<br>subjects affected / exposed          | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to<br>treatment / all           | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to<br>treatment / all                | 0 / 0           | 0 / 0           | 0 / 0           |
| General disorders and administration<br>site conditions      |                 |                 |                 |
| Chest pain<br>subjects affected / exposed                    | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to<br>treatment / all           | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to<br>treatment / all                | 0 / 0           | 0 / 0           | 0 / 0           |
| Immune system disorders                                      |                 |                 |                 |
| Immunisation reaction<br>subjects affected / exposed         | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to<br>treatment / all           | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to<br>treatment / all                | 0 / 0           | 0 / 0           | 0 / 0           |
| Reproductive system and breast<br>disorders                  |                 |                 |                 |
| Uterine polyp  |                 |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                            | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Respiratory, thoracic and mediastinal disorders</b> |                 |                 |                 |
| Acute respiratory failure                              |                 |                 |                 |
| subjects affected / exposed                            | 1 / 402 (0.25%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| Asthma   |                 |                 |                 |
| subjects affected / exposed                            | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumothorax   |                 |                 |                 |
| subjects affected / exposed                            | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Injury, poisoning and procedural complications</b>  |                 |                 |                 |
| Anaemia postoperative                                  |                 |                 |                 |
| subjects affected / exposed                            | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| Ankle fracture   |                 |                 |                 |
| subjects affected / exposed                            | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| Cervical vertebral fracture                            |                 |                 |                 |
| subjects affected / exposed                            | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| Fall   |                 |                 |                 |
| subjects affected / exposed                            | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Hip fracture                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Humerus fracture                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Joint dislocation                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ligament rupture                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Lisfranc fracture                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Post procedural haemorrhage                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Rib fracture                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 2 / 403 (0.50%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Road traffic accident                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Skin laceration                                 |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Spinal compression fracture                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Subdural haematoma                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Thoracic vertebral fracture                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Traumatic haemothorax                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Upper limb fracture                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac disorders                               |                 |                 |                 |
| Acute myocardial infarction                     |                 |                 |                 |
| subjects affected / exposed                     | 2 / 402 (0.50%) | 1 / 403 (0.25%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Angina pectoris                                 |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Angina unstable                                 |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Atrial fibrillation</b>                      |                 |                 |                 |
| subjects affected / exposed                     | 2 / 402 (0.50%) | 2 / 403 (0.50%) | 2 / 402 (0.50%) |
| occurrences causally related to treatment / all | 0 / 2           | 1 / 2           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Bradycardia</b>                              |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Cardiac failure acute</b>                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Cardiac failure congestive</b>               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 1 / 403 (0.25%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Myocardial infarction</b>                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 0           |
| <b>Myocardial ischaemia</b>                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Supraventricular tachycardia</b>             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Nervous system disorders</b>                 |                 |                 |                 |
| Cerebral artery thrombosis                      |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebral infarction                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebrovascular accident                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hepatic encephalopathy                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hyperaesthesia                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hyponatraemic encephalopathy                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ischaemic stroke                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Presyncope                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Spinal epidural haematoma                       |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Subarachnoid haemorrhage</b>                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Syncope</b>                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Eye disorders</b>                            |                 |                 |                 |
| <b>Cataract</b>                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Glaucoma</b>                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Gastrointestinal disorders</b>               |                 |                 |                 |
| <b>Abdominal pain</b>                           |                 |                 |                 |
| subjects affected / exposed                     | 3 / 402 (0.75%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 2 / 3           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Diarrhoea</b>                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (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           |
| <b>Diverticular perforation</b>                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Food poisoning</b>                           |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Gastric ulcer</b>                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (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           |
| <b>Gastritis</b>                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Inguinal hernia</b>                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Nausea</b>                                   |                 |                 |                 |
| subjects affected / exposed                     | 2 / 402 (0.50%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Obstructive pancreatitis</b>                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Small intestinal obstruction</b>             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Upper gastrointestinal haemorrhage</b>       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Vomiting</b>                                 |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 402 (0.00%) | 2 / 403 (0.50%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Hepatobiliary disorders</b>                  |                 |                 |                 |
| <b>Cholecystitis acute</b>                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Cholecystitis chronic</b>                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Cholelithiasis</b>                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Non-alcoholic steatohepatitis</b>            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Renal and urinary disorders</b>              |                 |                 |                 |
| <b>Acute kidney injury</b>                      |                 |                 |                 |
| subjects affected / exposed                     | 2 / 402 (0.50%) | 2 / 403 (0.50%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 3           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Bladder outlet obstruction</b>               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Stag horn calculus</b>                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Ureterolithiasis</b>                         |                 |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                            | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 2 / 402 (0.50%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Musculoskeletal and connective tissue disorders</b> |                 |                 |                 |
| <b>Neuropathic arthropathy</b>                         |                 |                 |                 |
| subjects affected / exposed                            | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Osteoarthritis</b>                                  |                 |                 |                 |
| subjects affected / exposed                            | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Pain in extremity</b>                               |                 |                 |                 |
| subjects affected / exposed                            | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Rotator cuff syndrome</b>                           |                 |                 |                 |
| subjects affected / exposed                            | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Spondylolisthesis</b>                               |                 |                 |                 |
| subjects affected / exposed                            | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Trigger finger</b>                                  |                 |                 |                 |
| subjects affected / exposed                            | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Infections and infestations</b>                     |                 |                 |                 |
| <b>Appendicitis</b>                                    |                 |                 |                 |
| subjects affected / exposed                            | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Bronchitis                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cellulitis                                      |                 |                 |                 |
| subjects affected / exposed                     | 2 / 402 (0.50%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Colonic abscess                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cystitis  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Diverticulitis                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Empyema   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastroenteritis                                 |                 |                 |                 |
| subjects affected / exposed                     | 3 / 402 (0.75%) | 3 / 403 (0.74%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 1 / 3           | 2 / 3           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Herpes zoster                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Joint abscess                                   |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Kidney infection</b>                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Osteomyelitis</b>                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Pharyngitis streptococcal</b>                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Pneumonia</b>                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 1 / 403 (0.25%) | 2 / 402 (0.50%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Pneumonia influenzal</b>                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Postoperative wound infection</b>            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Respiratory tract infection</b>              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Sepsis</b>                                   |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 3 / 402 (0.75%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Urosepsis</b>                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Viral infection</b>                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Wound infection staphylococcal</b>           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Metabolism and nutrition disorders</b>       |                 |                 |                 |
| <b>Cachexia</b>                                 |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Decreased appetite</b>                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (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           |
| <b>Dehydration</b>                              |                 |                 |                 |
| subjects affected / exposed                     | 2 / 402 (0.50%) | 1 / 403 (0.25%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 2           | 1 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Diabetes mellitus inadequate control</b>     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Diabetic ketoacidosis</b>                    |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Diabetic metabolic decompensation               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hyperglycaemia                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hyponatraemia                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ketoacidosis                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 1 / 403 (0.25%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Lactic acidosis                                 |                 |                 |                 |
| subjects affected / exposed                     | 1 / 402 (0.25%) | 0 / 403 (0.00%) | 0 / 402 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Obesity   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 402 (0.00%) | 0 / 403 (0.00%) | 1 / 402 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>  | Semaglutide 1.0 mg   | Semaglutide 2.4 mg   | Placebo   |
|--|--|--|---|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed   | 261 / 402 (64.93%)   | 284 / 403 (70.47%)   | 190 / 402 (47.26%)  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)   | 33 / 402 (8.21%)<br>48   | 31 / 403 (7.69%)<br>40   | 20 / 402 (4.98%)<br>27  |
| General disorders and administration site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)  | 19 / 402 (4.73%)<br>26   | 28 / 403 (6.95%)<br>29   | 4 / 402 (1.00%)<br>4  |
| Gastrointestinal disorders<br>Abdominal distension<br>subjects affected / exposed<br>occurrences (all)<br><br>Constipation<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Dyspepsia<br>subjects affected / exposed<br>occurrences (all)<br><br>Flatulence<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all) | 9 / 402 (2.24%)<br>12<br><br>51 / 402 (12.69%)<br>70<br><br>88 / 402 (21.89%)<br>157<br><br>27 / 402 (6.72%)<br>27<br><br>21 / 402 (5.22%)<br>25<br><br>128 / 402 (31.84%)<br>196<br><br>54 / 402 (13.43%)<br>93 | 24 / 403 (5.96%)<br>30<br><br>70 / 403 (17.37%)<br>82<br><br>86 / 403 (21.34%)<br>141<br><br>25 / 403 (6.20%)<br>30<br><br>16 / 403 (3.97%)<br>21<br><br>135 / 403 (33.50%)<br>248<br><br>86 / 403 (21.34%)<br>186 | 11 / 402 (2.74%)<br>13<br><br>22 / 402 (5.47%)<br>26<br><br>48 / 402 (11.94%)<br>66<br><br>5 / 402 (1.24%)<br>5<br><br>7 / 402 (1.74%)<br>9<br><br>37 / 402 (9.20%)<br>45<br><br>11 / 402 (2.74%)<br>12 |
| Musculoskeletal and connective tissue disorders<br>Arthralgia  |  |  |   |

|   |                         |                          |                         |
|---|-------------------------|--------------------------|-------------------------|
| subjects affected / exposed<br>occurrences (all)                                      | 24 / 402 (5.97%)<br>27  | 23 / 403 (5.71%)<br>29   | 20 / 402 (4.98%)<br>20  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)                         | 28 / 402 (6.97%)<br>30  | 27 / 403 (6.70%)<br>30   | 14 / 402 (3.48%)<br>15  |
| Infections and infestations   |                         |                          |                         |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)                   | 21 / 402 (5.22%)<br>25  | 11 / 403 (2.73%)<br>12   | 12 / 402 (2.99%)<br>14  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 47 / 402 (11.69%)<br>69 | 68 / 403 (16.87%)<br>115 | 59 / 402 (14.68%)<br>92 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 37 / 402 (9.20%)<br>54  | 42 / 403 (10.42%)<br>48  | 38 / 402 (9.45%)<br>50  |
| Metabolism and nutrition disorders  |                         |                          |                         |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                | 29 / 402 (7.21%)<br>33  | 38 / 403 (9.43%)<br>41   | 15 / 402 (3.73%)<br>17  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment   |
|--------------|---|
| 27 July 2018 | Inclusion of genetic biosamples for future analysis for applicable countries. Removal of discontinuation criteria for trial products for subjects enrolled in violation with exclusion/inclusion criteria. Removal of classification of risks, inclusion of a reference to the investigator's brochure. Removal of persistent criteria from exploratory endpoint regarding micro/macro albuminuria. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/33667417>

<http://www.ncbi.nlm.nih.gov/pubmed/32441473>

<http://www.ncbi.nlm.nih.gov/pubmed/30122305>