# Clinical trial results:
# Effect and safety of semaglutide 2.4 mg once-weekly in subjects with overweight or obesity

## Summary

| | |
|---|---|
| EudraCT number | 2017-003436-36 |
| Trial protocol | GB FI DK BG BE PL |
| Global end of trial date | 19 April 2020 |

**Results information**

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 19 February 2022 |
| First version publication date | 19 February 2022 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | NN9536-4373 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03548935 |
| WHO universal trial number (UTN) | U1111-1200-8053 |
| Other trial identifiers | JapicCTI: JapicCTI-183991 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Novo Nordisk A/S |
| Sponsor organisation address | Novo Allé, Bagsværd, Denmark, 2880 |
| Public contact | Clinical Reporting Office (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com |
| Scientific contact | Clinical Reporting Office (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 | 17 August 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 March 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 19 April 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.) 2.4 mg once-weekly versus semaglutide placebo as an adjunct to a reduced-calorie diet and increased physical activity in subjects with overweight or obesity on body weight.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013), the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice (2016) and Food and Drug Administration 21 Code of Federal Regulations 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? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Argentina: 65 |
| Country: Number of subjects enrolled | Belgium: 60 |
| Country: Number of subjects enrolled | Bulgaria: 45 |
| Country: Number of subjects enrolled | Canada: 63 |
| Country: Number of subjects enrolled | Germany: 100 |
| Country: Number of subjects enrolled | Denmark: 50 |
| Country: Number of subjects enrolled | Finland: 60 |
| Country: Number of subjects enrolled | France: 55 |
| Country: Number of subjects enrolled | United Kingdom: 218 |
| Country: Number of subjects enrolled | India: 117 |
| Country: Number of subjects enrolled | Japan: 100 |
| Country: Number of subjects enrolled | Mexico: 70 |
| Country: Number of subjects enrolled | Poland: 60 |
| Country: Number of subjects enrolled | Russian Federation: 100 |
| Country: Number of subjects enrolled | Taiwan: 35 |
| Country: Number of subjects enrolled | United States: 763 |

| | |
|---|---|
| Worldwide total number of subjects | 1961 |
| EEA total number of subjects | 430 |

Notes:

**Subjects enrolled per age group**

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 1805 |
| From 65 to 84 years | 155 |
| 85 years and over | 1 |

## Subject disposition

### Recruitment

Recruitment details:

The trial was conducted at 129 sites in 16 countries as follows: Argentina (5), Belgium (5), Bulgaria (5), Canada (7), Denmark (1), Finland (2), France (7), Germany (13), India (13), Japan (5), Mexico (3), Poland (4), Russian Federation (8), Taiwan (1), United Kingdom (10), United States (40).

### Pre-assignment

Screening details:

The trial included an initial 16-week dose-escalation period and a 52-week dose maintenance period. Subjects were randomized in 2:1 ratio either to receive semaglutide 2.4 mg or placebo. The treatment is an adjunct to reduced-calorie diet and increased physical activity.

### 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 |
| **Arm title** | Semaglutide 2.4 mg |

Arm description:

Subjects were to receive once-weekly subcutaneous (s.c) injection of Semaglutide using a PDS290 pre-filled pen-injector with a 3 mL cartridge containing Semaglutide 1.0 mg/mL or 3.0 mg/mL at a starting dose of 0.25 milligrams (mg) and then followed a fixed-dose escalation regimen, with dose increases every 4 weeks (to doses of 0.5, 1.0, 1.7 and 2.4 mg/week), aiming at reaching the maintenance dose of 2.4 mg after 16 weeks. Treatment was continued on the maintenance dose of 2.4 mg Semaglutide once-weekly for an additional 52 weeks until week 68. The treatment was an adjunct to a reduced-calorie diet and increased physical activity.

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

Dosage and administration details:

Once-weekly s.c injection of Semaglutide using a PDS290 pre-filled pen-injector with a 3 mL cartridge containing Semaglutide 3.0 mg/mL at a starting dose of 0.25 milligrams (mg) and then followed a fixed-dose escalation regimen, with dose increases every 4 weeks (to doses of 0.5, 1.0, 1.7 and 2.4 mg/week), aiming at reaching the maintenance dose of 2.4 mg after 16 weeks. Treatment was continued on the maintenance dose of 2.4 mg Semaglutide once-weekly for an additional 52 weeks until week 68. 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 1.0 mg/mL |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Once-weekly s.c injection of Semaglutide using a PDS290 pre-filled pen-injector with a 3 mL cartridge containing Semaglutide 1.0 mg/mL at a starting dose of 0.25 milligrams (mg) and then followed a fixed-

dose escalation regimen, with dose increases every 4 weeks (to doses of 0.5, 1.0, 1.7 and 2.4 mg/week), aiming at reaching the maintenance dose of 2.4 mg after 16 weeks. Treatment was continued on the maintenance dose of 2.4 mg Semaglutide once-weekly for an additional 52 weeks until week 68. Injections were administered in the thigh, abdomen or upper arm, and at any time of the day irrespective of meals.

| **Arm title** | Placebo |
|---|---|

Arm description:

Subjects were to receive once-weekly s.c injection of placebo matched to Semaglutide using a PDS290 pre-filled pen-injector with a 3 mL cartridge containing Semaglutide 1.0 mg/mL or 3.0 mg/mL for week 68. The treatment was an adjunct to a reduced-calorie diet and increased physical activity.

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

Dosage and administration details:

Once-weekly s.c injection of 0.25 mg Semaglutide placebo was administered using a PDS290 pre-filled pen-injector with a 3 mL cartridge. Dosing was once weekly with dose escalation every fourth week until the maintenance dose was reached. Injections could be administered in the thigh, abdomen or upper arm, and at any time of the day
irrespective of meals.

| **Number of subjects in period 1** | Semaglutide 2.4 mg | Placebo |
|---|---|---|
| Started | 1306 | 655 |
| Full analysis set (FAS) | 1306 | 655 |
| Safety analysis set (SAS) | 1306 | 655 |
| Completed | 1240 | 609 |
| Not completed | 66 | 46 |
| Adverse event, serious fatal | 1 | 1 |
| Consent withdrawn by subject | 26 | 17 |
| Lost to follow-up | 39 | 28 |

## Baseline characteristics

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

Reporting group description:

Subjects were to receive once-weekly subcutaneous (s.c) injection of Semaglutide using a PDS290 pre-filled pen-injector with a 3 mL cartridge containing Semaglutide 1.0 mg/mL or 3.0 mg/mL at a starting dose of 0.25 milligrams (mg) and then followed a fixed-dose escalation regimen, with dose increases every 4 weeks (to doses of 0.5, 1.0, 1.7 and 2.4 mg/week), aiming at reaching the maintenance dose of 2.4 mg after 16 weeks. Treatment was continued on the maintenance dose of 2.4 mg Semaglutide once-weekly for an additional 52 weeks until week 68. The treatment was an adjunct to a reduced-calorie diet and increased physical activity.

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

Reporting group description:

Subjects were to receive once-weekly s.c injection of placebo matched to Semaglutide using a PDS290 pre-filled pen-injector with a 3 mL cartridge containing Semaglutide 1.0 mg/mL or 3.0 mg/mL for week 68. The treatment was an adjunct to a reduced-calorie diet and increased physical activity.

| Reporting group values | Semaglutide 2.4 mg | Placebo | Total |
|---|---|---|---|
| Number of subjects | 1306 | 655 | 1961 |
| Age Categorical<br>Units: Subjects | | | |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 46 | 47 | |
| standard deviation | ± 13 | ± 12 | - |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 955 | 498 | 1453 |
| Male | 351 | 157 | 508 |

## End points

### End points reporting groups

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

Reporting group description:

Subjects were to receive once-weekly subcutaneous (s.c) injection of Semaglutide using a PDS290 pre-filled pen-injector with a 3 mL cartridge containing Semaglutide 1.0 mg/mL or 3.0 mg/mL at a starting dose of 0.25 milligrams (mg) and then followed a fixed-dose escalation regimen, with dose increases every 4 weeks (to doses of 0.5, 1.0, 1.7 and 2.4 mg/week), aiming at reaching the maintenance dose of 2.4 mg after 16 weeks. Treatment was continued on the maintenance dose of 2.4 mg Semaglutide once-weekly for an additional 52 weeks until week 68. The treatment was an adjunct to a reduced-calorie diet and increased physical activity.

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

Reporting group description:

Subjects were to receive once-weekly s.c injection of placebo matched to Semaglutide using a PDS290 pre-filled pen-injector with a 3 mL cartridge containing Semaglutide 1.0 mg/mL or 3.0 mg/mL for week 68. The treatment was an adjunct to a reduced-calorie diet and increased physical activity.

### Primary: Change in body weight (%)

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

End point description:

Change in body weight from baseline (week 0) to week 68 is presented. The endpoint was evaluated based on the data from both in-trial and on-treatment observation periods. In-trial observation period: the uninterrupted time interval from date of randomization (week 0) to date of last contact with trial site (week 75). On-treatment observation period: includes all time intervals in which subjects are considered to be on treatment from the first (week 0) to last trial product administration (week 68), including 2 weeks of follow-up. It excludes any period of temporary treatment interruption. Temporary treatment interruption is defined as more than 2 consecutive missed doses (off-treatment period). Full analysis set (FAS) included all randomised subjects according to the intention-to-treat principle.

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

End point timeframe:

From baseline at week 0 to week 68

| End point values | Semaglutide 2.4 mg | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1212 | 577 | | |
| Units: Percentage point | | | | |
| arithmetic mean (standard deviation) | | | | |
| In-trial observation period | -15.6 (± 10.1) | -2.8 (± 6.5) | | |
| On-treatment observation period | -16.9 (± 9.4) | -3.1 (± 6.4) | | |

### Statistical analyses

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

Statistical analysis description:

Analysis of data from in-trial period. ANCOVA: Week 68 responses were analysed using an analysis of covariance model with randomised treatment as factor and baseline body weight as covariate. RD-MI:

Missing observations were multiple (x1000) imputed from retrieved subjects of the same randomised treatment arm.
All subjects in FAS (1961 subjects) contributed to the analysis.

| | |
|---|---|
| Comparison groups | Semaglutide 2.4 mg v Placebo |
| Number of subjects included in analysis | 1789 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[1] |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Parameter estimate | Treatment difference |
| Point estimate | -12.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.37 |
| upper limit | -11.51 |

Notes:

[1] - Treatment policy estimand

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

Statistical analysis description:

Analysis of data from on-treatment period. Time-point considered as on-treatment if any dose of trial product has been administered within prior 14 days. MMRM: 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 with randomised treatment as factor and baseline body weight as covariate, all nested within visit.
All subjects in FAS (1961) contributed to the analysis.

| | |
|---|---|
| Comparison groups | Semaglutide 2.4 mg v Placebo |
| Number of subjects included in analysis | 1789 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[2] |
| P-value | < 0.0001 |
| Method | MMRM |
| Parameter estimate | Treatment difference |
| Point estimate | -14.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.29 |
| upper limit | -13.55 |

Notes:

[2] - Hypothetical estimand

## Primary: Subjects who achieve body weight reduction ≥ 5% (yes/no)

| End point title | Subjects who achieve body weight reduction ≥ 5% (yes/no) |
|---|---|

End point description:

Number of subjects who achieved weight loss more than or equal to 5% (yes/no) at week 68 are presented. The endpoint was evaluated based on the data from both in-trial and on-treatment observation periods. In-trial observation period: the uninterrupted time interval from start of randomization (week 0) to last trial-related subject-site contact (week 75). On-treatment observation period: includes all time intervals in which subjects are considered to be on treatment from the first (week 0) to last trial product administration (week 68), including 2 weeks of follow-up. It excludes any period of temporary treatment interruption. FAS included all randomised subjects according to the intention-to-treat principle.

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

End point timeframe:

After 68 weeks from baseline at week 0

| **End point values** | Semaglutide 2.4 mg | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1212 | 577 | | |
| Units: Subjects | | | | |
| In-trial observation period: Yes | 1047 | 182 | | |
| In-trial observation period: No | 165 | 395 | | |
| On-treatment observation period: Yes | 978 | 165 | | |
| On-treatment observation period: No | 81 | 334 | | |

## Statistical analyses

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

Statistical analysis description:

Analysis of data from on-treatment period. MMRM was performed on body weight (kg) and individual missing week 68 responses were predicted from the MMRM; each subject was then classified for body weight loss >= 5% and analysed using a binary logistic regression (LR) model with randomised treatment as factor and baseline body weight as covariate.
All subjects in FAS (1961 subjects) contributed to the analysis.

| Comparison groups | Semaglutide 2.4 mg v Placebo |
|---|---|
| Number of subjects included in analysis | 1789 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[3] |
| P-value | < 0.0001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 37.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 28.02 |
| upper limit | 48.95 |

Notes:

[3] - Hypothetical estimand

| **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 as factor and baseline body weight as covariate. RD-MI: Missing observations were multiple (x1000) imputed from retrieved subjects of the same randomised treatment arm.
All subjects in FAS (1961 subjects) contributed to the analysis.

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

| | |
|---|---|
| Number of subjects included in analysis | 1789 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[4] |
| P-value | < 0.0001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 11.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 8.88 |
| upper limit | 14.19 |

Notes:

[4] - Treatment policy estimand

## Secondary: Subjects who achieve (yes/no) body weight reduction ≥ 10%

| | |
|---|---|
| End point title | Subjects who achieve (yes/no) body weight reduction ≥ 10% |

End point description:

Number of subjects who achieved weight loss more than or equal to (≥) 10% at week 68 is presented. The endpoint was evaluated based on the data from in-trial observation period. In-trial observation period: the uninterrupted time interval from date of randomization (week 0) to date of last contact with trial site (week 75). FAS included all randomised subjects according to the intention-to-treat principle.

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

End point timeframe:

After 68 weeks from baseline at week 0

| End point values | Semaglutide 2.4 mg | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1212 | 577 | | |
| Units: Subjects | | | | |
| Yes | 838 | 69 | | |
| No | 374 | 508 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Subjects who achieve (yes/no) body weight reduction ≥ 15%

| | |
|---|---|
| End point title | Subjects who achieve (yes/no) body weight reduction ≥ 15% |

End point description:

Number of subjects who achieved more than or equal to (≥) 15% weight loss at week 68 is presented. The endpoint was evaluated based on the data from in-trial observation period. In-trial observation period: the uninterrupted time interval from start of randomization (week 0) to last trial-related subject-site contact (week 75). FAS included all randomised subjects according to the intention-to-treat principle.

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

End point timeframe:

After 68 weeks from baseline at week 0

| End point values | Semaglutide 2.4 mg | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1212 | 577 | | |
| Units: Subjects | | | | |
| Yes | 612 | 28 | | |
| No | 600 | 549 | | |

## 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. The endpoint was evaluated based on the data from in-trial observation period. In-trial observation period: the uninterrupted time interval from start of randomization (week 0) to date of last contact with trial site (week 75). FAS included all randomised subjects according to the intention-to-treat principle.

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

End point timeframe:

From baseline at week 0 to week 68

| End point values | Semaglutide 2.4 mg | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1210 | 575 | | |
| Units: Centimeter (cm) | | | | |
| arithmetic mean (standard deviation) | -14.1 (± 9.6) | -4.4 (± 6.9) | | |

## 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. The endpoint was evaluated based on the data from in-trial observation period. In-trial observation period: the uninterrupted time interval from start of randomization (week 0) to date of last contact with trial site

(week 75). FAS included all randomised subjects according to the intention-to-treat principle.

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

End point timeframe:

From baseline at week 0 to week 68

| End point values | Semaglutide 2.4 mg | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1210 | 574 | | |
| Units: Millimeters of mercury (mmHg) | | | | |
| arithmetic mean (standard deviation) | -7 (± 14) | -1 (± 13) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change in Physical functioning score (SF-36)

| End point title | Change in Physical functioning score (SF-36) |
|---|---|

End point description:

Short Form 36 version 2.0 acute (SF-36) is a 36-item patient-reported survey of patient health that measures the participant's overall health-related quality of life (HRQoL). SF-36v2™ questionnaire measured eight domains of functional health and well-being as well as two component summary scores (physical component summary and mental component summary). In the metric of norm-based scores, 50 and 10 corresponds to the mean and standard deviation, respectively, for the 2009 US general population. 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. The endpoint was evaluated based on the data from in-trial observation period which is the uninterrupted time interval from start of randomization (week 0) to last trial-related subject-site contact (week 75). FAS included all randomised subjects according to the intention-to-treat principle.

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

End point timeframe:

From baseline at week 0 to week 68

| End point values | Semaglutide 2.4 mg | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1195 | 566 | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | 2.3 (± 6.6) | 0.4 (± 7.4) | | |

### Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Impact of Weight on Quality of Life-Lite for Clinical Trials (IWQoL-Lite-CT) is a modified version of an instrument designed to assess weight-related quality of life. It is used to assess the impact of body weight changes on patients' physical and psychosocial functioning in three composite scores (physical function, physical and psychosocial) and a total score. The scores range between 0-100 where higher scores indicate a better quality of life. A positive change score indicates an improvement since baseline. This endpoint was evaluated based on the data from in-trial observation period which is the uninterrupted time interval from start of randomization (week 0) to last trial-related subject-site contact (week 75). FAS included all randomised subjects according to the intention-to-treat principle.

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

End point timeframe:

From baseline at week 0 to week 68

| **End point values** | Semaglutide 2.4 mg | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1193 | 566 | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | 15.0 (± 21.6) | 6.0 (± 21.1) | | |

### 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 participants who received at least one dose of Semaglutide or placebo.

Adverse event reporting additional description:

All AEs mentioned here are TEAE defined as an event that had onset date (or increase in severity) on or after the first day of exposure to randomized treatment and no later than the date of last dose + 7 weeks.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 22 |

### Reporting groups

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

Reporting group description:

Subjects were to receive once-weekly s.c injection of placebo matched to Semaglutide using a PDS290 pre-filled pen-injector with a 3 mL cartridge containing Semaglutide 1.0 mg/mL or 3.0 mg/mL for week 68. The treatment was an adjunct to a reduced-calorie diet and increased physical activity.

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

Reporting group description:

Subjects were to receive once-weekly subcutaneous (s.c) injection of Semaglutide using a PDS290 pre-filled pen-injector with a 3 mL cartridge containing Semaglutide 1.0 mg/mL or 3.0 mg/mL at a starting dose of 0.25 milligrams (mg) and then followed a fixed-dose escalation regimen, with dose increases every 4 weeks (to doses of 0.5, 1.0, 1.7 and 2.4 mg/week), aiming at reaching the maintenance dose of 2.4 mg after 16 weeks. Treatment was continued on the maintenance dose of 2.4 mg Semaglutide once-weekly for an additional 52 weeks until week 68. The treatment was an adjunct to a reduced-calorie diet and increased physical activity.

| **Serious adverse events** | Placebo | Semaglutide 2.4 mg | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 42 / 655 (6.41%) | 128 / 1306 (9.80%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cervix carcinoma stage 0 | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal stromal tumour | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Glioblastoma | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hairy cell leukaemia | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intraductal proliferative breast lesion | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 2 / 1306 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leiomyoma | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian adenoma | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |

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|---|---|---|---|
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Abdominoplasty | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone prosthesis insertion | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystectomy | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric bypass | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip surgery | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc operation | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal | | | |

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|---|---|---|---|
| conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 2 / 1306 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 2 / 1306 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular stent occlusion | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Dysfunctional uterine bleeding | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erectile dysfunction | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine haemorrhage | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma | | | |
| subjects affected / exposed | 2 / 655 (0.31%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasal polyps | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleurisy | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 655 (0.31%) | 2 / 1306 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsillar hypertrophy | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Acute stress disorder | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide attempt | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Weight increased | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural | | | |

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|---|---|---|---|
| complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gun shot wound | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ligament rupture | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meniscus injury | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 2 / 1306 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 655 (0.15%) | 2 / 1306 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial tachycardia | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiomyopathy | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 2 / 655 (0.31%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocarditis | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cranial nerve disorder | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Idiopathic intracranial hypertension | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nerve compression | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peroneal nerve palsy | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychogenic seizure | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo CNS origin | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Blood and lymphatic system disorders** | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 2 / 1306 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Splenic haemorrhage | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Ear and labyrinth disorders** | | | |
| Meniere's disease | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 3 / 1306 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Eye disorders** | | | |
| Diplopia | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Optic ischaemic neuropathy | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 2 / 1306 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|---|---|---|
| Gastrointestinal disorders | | | |
| Abdominal hernia | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 3 / 1306 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal fistula | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 2 / 1306 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis ischaemic | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enteritis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 2 / 1306 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal achalasia | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 2 / 1306 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 4 / 1306 (0.31%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Volvulus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Bile duct stone | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 4 / 1306 (0.31%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 3 / 1306 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 12 / 1306 (0.92%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Actinic keratosis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hidradenitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Calculus urinary | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthropathy | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Costochondritis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myalgia intercostal | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 2 / 655 (0.31%) | 3 / 1306 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 5 / 1306 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis perforated | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis infective | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial colitis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic sinusitis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Empyema | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 655 (0.00%) | 5 / 1306 (0.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis astroviral | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis E | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine infection | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis viral | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 655 (0.31%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 2 / 1306 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxoplasmosis | | | |
| subjects affected / exposed | 1 / 655 (0.15%) | 0 / 1306 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Gout | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 655 (0.00%) | 1 / 1306 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Placebo | Semaglutide 2.4 mg | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 447 / 655 (68.24%) | 1052 / 1306 (80.55%) | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 23 / 655 (3.51%) | 98 / 1306 (7.50%) | |
| occurrences (all) | 35 | 129 | |
| Headache | | | |
| subjects affected / exposed | 80 / 655 (12.21%) | 198 / 1306 (15.16%) | |
| occurrences (all) | 104 | 386 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 28 / 655 (4.27%) | 104 / 1306 (7.96%) | |
| occurrences (all) | 29 | 120 | |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| Abdominal distension | | | |
| subjects affected / exposed | 31 / 655 (4.73%) | 96 / 1306 (7.35%) | |
| occurrences (all) | 42 | 135 | |
| Abdominal pain | | | |
| subjects affected / exposed | 36 / 655 (5.50%) | 127 / 1306 (9.72%) | |
| occurrences (all) | 41 | 172 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 35 / 655 (5.34%) | 125 / 1306 (9.57%) | |
| occurrences (all) | 37 | 176 | |
| Constipation | | | |
| subjects affected / exposed | 62 / 655 (9.47%) | 305 / 1306 (23.35%) | |
| occurrences (all) | 73 | 389 | |
| Diarrhoea | | | |
| subjects affected / exposed | 104 / 655 (15.88%) | 411 / 1306 (31.47%) | |
| occurrences (all) | 138 | 765 | |
| Dyspepsia | | | |
| subjects affected / exposed | 23 / 655 (3.51%) | 135 / 1306 (10.34%) | |
| occurrences (all) | 30 | 179 | |
| Eructation | | | |
| subjects affected / exposed | 3 / 655 (0.46%) | 112 / 1306 (8.58%) | |
| occurrences (all) | 3 | 139 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 20 / 655 (3.05%) | 82 / 1306 (6.28%) | |
| occurrences (all) | 21 | 92 | |
| Nausea | | | |
| subjects affected / exposed | 114 / 655 (17.40%) | 576 / 1306 (44.10%) | |
| occurrences (all) | 146 | 1067 | |
| Vomiting | | | |
| subjects affected / exposed | 43 / 655 (6.56%) | 321 / 1306 (24.58%) | |
| occurrences (all) | 52 | 632 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 33 / 655 (5.04%) | 40 / 1306 (3.06%) | |
| occurrences (all) | 35 | 45 | |
| Musculoskeletal and connective tissue | | | |

| | | | |
|---|---|---|---|
| disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 53 / 655 (8.09%) | 106 / 1306 (8.12%) | |
| occurrences (all) | 55 | 120 | |
| Arthralgia | | | |
| subjects affected / exposed | 43 / 655 (6.56%) | 81 / 1306 (6.20%) | |
| occurrences (all) | 47 | 92 | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 30 / 655 (4.58%) | 81 / 1306 (6.20%) | |
| occurrences (all) | 38 | 99 | |
| Influenza | | | |
| subjects affected / exposed | 63 / 655 (9.62%) | 89 / 1306 (6.81%) | |
| occurrences (all) | 79 | 112 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 133 / 655 (20.31%) | 281 / 1306 (21.52%) | |
| occurrences (all) | 216 | 480 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 80 / 655 (12.21%) | 114 / 1306 (8.73%) | |
| occurrences (all) | 116 | 158 | |
| Sinusitis | | | |
| subjects affected / exposed | 36 / 655 (5.50%) | 70 / 1306 (5.36%) | |
| occurrences (all) | 40 | 83 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 28 / 655 (4.27%) | 68 / 1306 (5.21%) | |
| occurrences (all) | 33 | 83 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 22 / 655 (3.36%) | 124 / 1306 (9.49%) | |
| occurrences (all) | 26 | 139 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 04 July 2018 | Implementation of genetic biosamples for future analysis for those countries where it will be applicable. Removal of criteria for discontinuation of trial treatment for subjects included in the trial in violation of the inclusion and/or exclusion criteria and/or randomisation criteria. Classifications of risks have been removed from the protocol and instead a reference to the investigator's brochure or any updates hereof has been added for further details of the risks associated with semaglutide treatment. |
| 09 May 2019 | Trial extension: 52-weeks off-treatment period after end of treatment in the main phase without structured lifestyle intervention in the following countries only: Canada, Germany, the UK and selected sites in the US and Japan. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

### Online references

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

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

http://www.ncbi.nlm.nih.gov/pubmed/33567185