



Clinical trial results:

Efficacy and Safety of Oral Semaglutide versus Placebo in Subjects with Type 2 Diabetes Mellitus treated with insulin - A 52-week, randomised, placebo-controlled trial, double-blinded during the initial 26 weeks.

Summary

EudraCT number	2016-000988-16
Trial protocol	FR GR PL
Global end of trial date	22 August 2018

Results information

Result version number	v1 (current)
This version publication date	05 September 2019
First version publication date	05 September 2019

Trial information

Trial identification

Sponsor protocol code	NN9924-4280
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03021187
WHO universal trial number (UTN)	U1111-1180-3637

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting 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	12 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 January 2018
Global end of trial reached?	Yes
Global end of trial date	22 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the effect of once-daily dosing of three dose levels of oral semaglutide (3 mg, 7 mg and 14 mg) versus placebo on glycaemic control in subjects with type 2 diabetes mellitus treated with insulin.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2013), ICH Good Clinical Practice, including archiving of essential documents (1996), and 21 CFR 312.120.

Background therapy:

The subjects continued to receive their regular dose of insulin throughout the trial. The 52-week randomised treatment period was split into two treatment periods; an initial 26-week fixed insulin treatment period where the insulin treatment was restricted, followed by a 26-week period where the insulin treatment was adjustable without any restrictions.

Evidence for comparator:

Not applicable

Actual start date of recruitment	02 February 2017
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	Canada: 41
Country: Number of subjects enrolled	France: 38
Country: Number of subjects enrolled	Greece: 31
Country: Number of subjects enrolled	India: 51
Country: Number of subjects enrolled	Japan: 194
Country: Number of subjects enrolled	Mexico: 40
Country: Number of subjects enrolled	Poland: 65
Country: Number of subjects enrolled	Russian Federation: 61
Country: Number of subjects enrolled	United States: 210
Worldwide total number of subjects	731
EEA total number of subjects	134

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)	453
From 65 to 84 years	276
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 111 sites in 9 countries: Canada (7), France (10), Greece (6), India (9), Japan (18), Mexico (2), Poland (4), Russian Federation (5) and United States (48). Following sites were approved by the IRB/IEC but didn't randomise subjects: France (2), India (1), Japan (1) and United States (3).

Pre-assignment

Screening details:

Not applicable

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Oral semaglutide 3 mg

Arm description:

Subjects were randomised to receive once-daily semaglutide 3 mg tablets for a period of 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Semaglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were to take the 3 mg semaglutide tablets once daily in the morning in a fasting state and at least 30 minutes before the first meal of the day for 52 weeks. The tablet was to be taken with about 120 ml (half a glass) of water. Subjects had to swallow the tablet as a whole and not break or chew it. Oral medication other than trial product could be taken 30 minutes after administration of trial product.

Arm title	Oral semaglutide 7 mg
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Arm description:

Subjects were randomised to receive once-daily semaglutide tablet in a dose escalation manner for 52 weeks: 3 mg from weeks 1-4 and 7 mg from weeks 5-52.

Arm type	Experimental
Investigational medicinal product name	Semaglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were to take 3 mg semaglutide tablets once daily in the morning in a fasting state for first 4 weeks. They were to take 7 mg semaglutide tablets for the rest of the treatment period upto 52 weeks. The tablet was to be taken at least 30 minutes before the first meal of the day with about 120 ml (half a glass) of water. Subjects had to swallow the tablet as a whole and not break or chew it. Oral medication other than trial product could be taken 30 minutes after administration of trial product.

Arm title	Oral semaglutide 14 mg
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Arm description:

Subjects were randomised to receive once-daily semaglutide tablets in a dose escalation manner for 52 weeks: 3 mg from weeks 1-4, 7 mg from weeks 5-8 and 14 mg from weeks 9-52.

Arm type	Experimental
Investigational medicinal product name	Semaglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were to take 3 mg semaglutide for first 4 weeks followed by 7 mg tablets for another 4 weeks and then 14 mg tablets for the rest of the treatment period upto 52 weeks in the fasting state. The tablet was to be taken at least 30 minutes before the first meal of the day with about 120 ml (half a glass) of water. Subjects had to swallow the tablet as a whole and not break or chew it. Oral medication other than trial product could be taken 30 minutes after administration of trial product.

Arm title	Placebo
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Arm description:

Subjects were randomised to receive once-daily placebo tablets for a period of 52 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects in the placebo group were to take placebo tablets once daily in the morning in a fasting state for 52 weeks. The tablet was to be taken with about 120 ml (half a glass) of water. Subjects had to swallow the tablet as a whole and not break or chew it. Oral medication other than trial product could be taken 30 minutes after administration of trial product.

Number of subjects in period 1	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg
Started	184	182	181
Exposed	184	181	181
Completed	174	173	175
Not completed	10	9	6
Adverse event, serious fatal	-	-	3
Consent withdrawn by subject	-	6	2
Lost to follow-up	10	3	1

Number of subjects in period 1	Placebo
Started	184
Exposed	184
Completed	175
Not completed	9
Adverse event, serious fatal	-
Consent withdrawn by subject	5
Lost to follow-up	4

Baseline characteristics

Reporting groups

Reporting group title	Oral semaglutide 3 mg
Reporting group description:	
Subjects were randomised to receive once-daily semaglutide 3 mg tablets for a period of 52 weeks.	
Reporting group title	Oral semaglutide 7 mg
Reporting group description:	
Subjects were randomised to receive once-daily semaglutide tablet in a dose escalation manner for 52 weeks: 3 mg from weeks 1-4 and 7 mg from weeks 5-52.	
Reporting group title	Oral semaglutide 14 mg
Reporting group description:	
Subjects were randomised to receive once-daily semaglutide tablets in a dose escalation manner for 52 weeks: 3 mg from weeks 1-4, 7 mg from weeks 5-8 and 14 mg from weeks 9-52.	
Reporting group title	Placebo
Reporting group description:	
Subjects were randomised to receive once-daily placebo tablets for a period of 52 weeks.	

Reporting group values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg
Number of subjects	184	182	181
Age Categorical Units: Subjects			
Adults (18 to 65 years)	110	121	108
From 65 to 75 years	67	49	60
From 75 to 85 years	7	12	11
85 years and above	0	0	2
Age Continuous Units: years			
arithmetic mean	61	60	61
standard deviation	± 9	± 10	± 10
Gender Categorical Units: Subjects			
Female	82	79	96
Male	102	103	85
HbA1c			
Glycosylated haemoglobin			
Units: %-points			
arithmetic mean	8.2	8.2	8.2
standard deviation	± 0.7	± 0.7	± 0.7

Reporting group values	Placebo	Total	
Number of subjects	184	731	
Age Categorical Units: Subjects			
Adults (18 to 65 years)	114	453	
From 65 to 75 years	63	239	
From 75 to 85 years	7	37	
85 years and above	0	2	

Age Continuous			
Units: years			
arithmetic mean	60		
standard deviation	± 10	-	
Gender Categorical			
Units: Subjects			
Female	79	336	
Male	105	395	
HbA1c			
Glycosylated haemoglobin			
Units: %-points			
arithmetic mean	8.2		
standard deviation	± 0.7	-	

End points

End points reporting groups

Reporting group title	Oral semaglutide 3 mg
Reporting group description: Subjects were randomised to receive once-daily semaglutide 3 mg tablets for a period of 52 weeks.	
Reporting group title	Oral semaglutide 7 mg
Reporting group description: Subjects were randomised to receive once-daily semaglutide tablet in a dose escalation manner for 52 weeks: 3 mg from weeks 1-4 and 7 mg from weeks 5-52.	
Reporting group title	Oral semaglutide 14 mg
Reporting group description: Subjects were randomised to receive once-daily semaglutide tablets in a dose escalation manner for 52 weeks: 3 mg from weeks 1-4, 7 mg from weeks 5-8 and 14 mg from weeks 9-52.	
Reporting group title	Placebo
Reporting group description: Subjects were randomised to receive once-daily placebo tablets for a period of 52 weeks.	

Primary: Change in HbA1c (in-trial observation period: week 26)

End point title	Change in HbA1c (in-trial observation period: week 26)
End point description: Mean change from baseline (week 0) to week 26 in glycosylated haemoglobin (HbA1c). The endpoint was evaluated based on data from the in-trial observation period. In-trial observation period started at the date of randomisation and included the period after initiation of rescue medication and/or premature trial product discontinuation, if any. Analysis population: Full analysis set which comprised all randomised subjects. "Number of subjects analysed" = subjects with available data.	
End point type	Primary
End point timeframe: From baseline to week 26	

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	176	174	173	176
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-0.5 (± 1.0)	-1.0 (± 1.1)	-1.3 (± 1.1)	-0.1 (± 0.9)

Statistical analyses

Statistical analysis title	Semaglutide 3 mg vs Placebo
Statistical analysis description: Missing post-baseline values were imputed by a pattern mixture model using multiple imputation. Imputation was from own treatment arm and same treatment status. Change from baseline was analysed using an analysis of covariance (ANCOVA) model with treatment, strata, interaction strata, and region as categorical fixed effects and baseline value as covariate for each of the 1000 imputed complete datasets, and pooled by Rubin's rule to draw inference.	

Comparison groups	Oral semaglutide 3 mg v Placebo
Number of subjects included in analysis	352
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	< 0.0001 ^[2]
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.3

Notes:

[1] - This hypothesis was controlled for multiplicity. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand). Number of subjects included in analysis = Number of subjects in the FAS, who contributed to the analysis.

[2] - Unadjusted two-sided p-value for test of no difference from 0.

Statistical analysis title	Semaglutide 7 mg vs Placebo
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Statistical analysis description:

Missing post-baseline values were imputed by a pattern mixture model using multiple imputation. Imputation was from own treatment arm and same treatment status. Change from baseline was analysed using an ANCOVA model with treatment, strata, interaction strata and region as categorical fixed effects and baseline value as covariate for each of the 1000 imputed complete datasets, and pooled by Rubin's rule to draw inference.

Comparison groups	Oral semaglutide 7 mg v Placebo
Number of subjects included in analysis	350
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	< 0.0001 ^[4]
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.7

Notes:

[3] - This hypothesis was controlled for multiplicity. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand). Number of subjects included in analysis = Number of subjects in the FAS, who contributed to the analysis.

[4] - Unadjusted two-sided p-value for test of no difference from 0.

Statistical analysis title	Semaglutide 14 mg vs Placebo
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Statistical analysis description:

Missing post-baseline values were imputed by a pattern mixture model using multiple imputation. Imputation was from own treatment arm and same treatment status. Change from baseline was analysed using an ANCOVA model with treatment, strata, interaction strata and region as categorical fixed effects and baseline value as covariate for each of the 1000 imputed complete datasets, and pooled by Rubin's rule to draw inference.

Comparison groups	Oral semaglutide 14 mg v Placebo
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Number of subjects included in analysis	349
Analysis specification	Pre-specified
Analysis type	superiority ^[5]
P-value	< 0.0001 ^[6]
Method	ANCOVA
Parameter estimate	Treatment difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-1

Notes:

[5] - This hypothesis was controlled for multiplicity. The estimated treatment effect includes the effect of any rescue medication and any effect after premature trial product discontinuation (treatment policy estimand). Number of subjects included in analysis = Number of subjects in the FAS, who contributed to the analysis.

[6] - Unadjusted two-sided p-value for test of no difference from 0.

Primary: Change in HbA1c (on-treatment without rescue medication observation period: week 26)

End point title	Change in HbA1c (on-treatment without rescue medication observation period: week 26)
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End point description:

Mean change from baseline (week 0) to week 26 in HbA1c. The endpoint was analysed based on data from the on-treatment without rescue medication observation period. On-treatment without rescue medication observation period started at the date of the first dose of trial product and includes the period after initiation of rescue medication, if any, and excludes the period after premature trial discontinuation, if any. Analysis population: Full analysis set which comprised all randomised subjects. "Number of subjects analysed" = subjects with available data.

End point type	Primary
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End point timeframe:

From baseline to week 26

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	162	157	146	161
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-0.6 (± 1.1)	-1.1 (± 1.0)	-1.4 (± 0.9)	-0.1 (± 0.8)

Statistical analyses

Statistical analysis title	Semaglutide 3 mg vs Placebo
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Statistical analysis description:

Changes from baseline were analysed using a mixed model for repeated measurements model with treatment, strata, interaction strata, and region as categorical fixed effects and baseline value as covariate, all nested within visit, and an unstructured residual covariance matrix.

Comparison groups	Oral semaglutide 3 mg v Placebo
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Number of subjects included in analysis	323
Analysis specification	Pre-specified
Analysis type	superiority ^[7]
P-value	< 0.0001 ^[8]
Method	Mixed model for repeated measurements
Parameter estimate	Treatment difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.4

Notes:

[7] - Analysis was based on hypothetical estimand. This hypothesis was not controlled for multiplicity. "Subjects in this analysis"=number of subjects with available data; all subjects in the FAS with data contributed to the analysis.

[8] - Unadjusted two-sided p-value for test of no difference from 0.

Statistical analysis title	Semaglutide 7 mg vs Placebo
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Statistical analysis description:

Changes from baseline were analysed using a mixed model for repeated measurements model with treatment, strata, interaction strata, and region as categorical fixed effects and baseline value as covariate, all nested within visit, and an unstructured residual covariance matrix.

Comparison groups	Oral semaglutide 7 mg v Placebo
Number of subjects included in analysis	318
Analysis specification	Pre-specified
Analysis type	superiority ^[9]
P-value	< 0.0001 ^[10]
Method	Mixed model for repeated measurements
Parameter estimate	Treatment difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.8

Notes:

[9] - Analysis was based on hypothetical estimand. This hypothesis was not controlled for multiplicity. "Subjects in this analysis"=number of subjects with available data; all subjects in the FAS with data contributed to the analysis.

[10] - Unadjusted two-sided p-value for test of no difference from 0.

Statistical analysis title	Semaglutide 14 mg vs Placebo
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Statistical analysis description:

Changes from baseline were analysed using a mixed model for repeated measurements model with treatment, strata, interaction strata, and region as categorical fixed effects and baseline value as covariate, all nested within visit, and an unstructured residual covariance matrix.

Comparison groups	Oral semaglutide 14 mg v Placebo
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Number of subjects included in analysis	307
Analysis specification	Pre-specified
Analysis type	superiority ^[11]
P-value	< 0.0001 ^[12]
Method	Mixed model for repeated measurements
Parameter estimate	Treatment difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-1.2

Notes:

[11] - Analysis was based on hypothetical estimand. This hypothesis was not controlled for multiplicity. "Subjects in this analysis"=number of subjects with available data; all subjects in the FAS with data contributed to the analysis.

[12] - Unadjusted two-sided p-value for test of no difference from 0.

Secondary: Change in body weight (kg) (in-trial observation period: week 26)

End point title	Change in body weight (kg) (in-trial observation period: week 26)
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End point description:

Change from baseline (week 0) in body weight to week 26. The endpoint was evaluated based on data from the in-trial observation period. In-trial observation period started at the date of randomisation and included the period after initiation of rescue medication and/or premature trial product discontinuation, if any. Analysis population: Full analysis set which comprised all randomised subjects. "Number of subjects analysed" = subjects with available data.

End point type	Secondary
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End point timeframe:

From baseline to 26 weeks

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	177	174	173	177
Units: kilograms (kg)				
arithmetic mean (standard deviation)	-1.4 (± 3.1)	-2.6 (± 5.2)	-3.7 (± 4.0)	-0.5 (± 2.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body weight (kg) (on-treatment period without rescue medication observation period: week 26)

End point title	Change in body weight (kg) (on-treatment period without rescue medication observation period: week 26)
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End point description:

Mean change from baseline to week 26 in body weight. The endpoint was evaluated based on data from the on-treatment without rescue medication observation period. On-treatment without rescue

medication observation period started at the date of the first dose of trial product and included the period after initiation of rescue medication, if any, and excluded the period after premature trial discontinuation, if any. Analysis population: Full analysis set which comprised all randomised subjects. "Number of subjects analysed" = subjects with available data.

End point type	Secondary
End point timeframe:	
From baseline to week 26	

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	163	157	146	162
Units: kg				
arithmetic mean (standard deviation)	-1.5 (± 3.1)	-3.0 (± 3.7)	-3.9 (± 3.6)	-0.5 (± 2.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in HbA1c (week 52)

End point title	Change in HbA1c (week 52)
End point description:	
Change from baseline (week 0) in HbA1c to week 52. The endpoint was evaluated based on data from the in-trial observation period. In trial observation period started at the date of randomisation and included the period after initiation of rescue medication and/or premature trial product discontinuation, if any. Analysis population: Full analysis set which comprised all randomised subjects. "Number of subjects analysed" = subjects with available data.	
End point type	Secondary
End point timeframe:	
From baseline to week 52	

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	173	169	168	172
Units: Percentage of HbA1c				
arithmetic mean (standard deviation)	-0.6 (± 1.0)	-0.9 (± 1.1)	-1.2 (± 1.0)	-0.2 (± 0.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in body weight (kg) (week 52)

End point title	Change in body weight (kg) (week 52)
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End point description:

Change from baseline (week 0) in body weight to week 52. The endpoint was evaluated based on data from the in-trial observation period. In trial observation period started at the date of randomisation and included the period after initiation of rescue medication and/or premature trial product discontinuation, if any. Analysis population: Full analysis set which comprised all randomised subjects. "Number of subjects analysed" = subjects with available data.

End point type	Secondary
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End point timeframe:

From baseline to week 52

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	174	171	170	173
Units: kg				
arithmetic mean (standard deviation)	-0.9 (± 3.9)	-2.2 (± 5.2)	-3.8 (± 5.8)	0.5 (± 3.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting plasma glucose (FPG) (week 26)

End point title	Change in fasting plasma glucose (FPG) (week 26)
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End point description:

Change from baseline (week 0) in fasting plasma glucose to week 26. The endpoint was evaluated based on data from the in-trial observation period. In trial observation period started at the date of randomisation and included the period after initiation of rescue medication and/or premature trial product discontinuation, if any. Analysis population: Full analysis set which comprised all randomised subjects. "Number of subjects analysed" = subjects with available data.

End point type	Secondary
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End point timeframe:

From baseline to week 26

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	175	173	173	175
Units: mmol/L				
arithmetic mean (standard deviation)	-0.45 (± 3.35)	-1.14 (± 3.08)	-1.36 (± 2.72)	0.51 (± 2.84)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting plasma glucose (FPG) (week 52)

End point title	Change in fasting plasma glucose (FPG) (week 52)
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End point description:

Change from baseline (week 0) in fasting plasma glucose to week 52. The endpoint was evaluated based on data from the in-trial observation period. In trial observation period started at the date of randomisation and included the period after initiation of rescue medication and/or premature trial product discontinuation, if any. Analysis population: Full analysis set which comprised all randomised subjects. "Number of subjects analysed" = subjects with available data.

End point type	Secondary
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End point timeframe:

From baseline to week 52

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	172	168	169	172
Units: mmol/L				
arithmetic mean (standard deviation)	-0.81 (± 3.21)	-1.12 (± 2.91)	-1.60 (± 2.65)	-0.09 (± 2.97)

Statistical analyses

No statistical analyses for this end point

Secondary: If a subject achieves (yes/no): HbA1c < 7.0% (53 mmol/mol) (American Diabetes Association (ADA) target) (week 26)

End point title	If a subject achieves (yes/no): HbA1c < 7.0% (53 mmol/mol) (American Diabetes Association (ADA) target) (week 26)
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End point description:

Number of subjects achieving HbA1c < 7.0 % (53 mmol/mol) according to American Diabetes Association (ADA) target, at week 26. The endpoint was evaluated based on data from the in-trial observation period. In trial observation period started at the date of randomisation and included the period after initiation of rescue medication and/or premature trial product discontinuation, if any. Analysis population: Full analysis set which comprised all randomised subjects. "Number of subjects analysed" = subjects with available data.

End point type	Secondary
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End point timeframe:

After week 26

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	176	174	173	176
Units: Subjects				
Yes	50	74	101	12
No	126	100	72	164

Statistical analyses

No statistical analyses for this end point

Secondary: If a subject achieves (yes/no): HbA1c < 7.0% (53 mmol/mol) (American Diabetes Association (ADA) target) (week 52)

End point title	If a subject achieves (yes/no): HbA1c < 7.0% (53 mmol/mol) (American Diabetes Association (ADA) target) (week 52)
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End point description:

Number of subjects achieving HbA1c < 7.0 % (53 mmol/mol) according to the ADA target, at week 52. The endpoint was evaluated based on data from the in-trial observation period. In trial observation period started at the date of randomisation and included the period after initiation of rescue medication and/or premature trial product discontinuation, if any. Analysis population: Full analysis set which comprised all randomised subjects. "Number of subjects analysed" = subjects with available data.

End point type	Secondary
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End point timeframe:

After week 52

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	173	169	168	172
Units: Subjects				
Yes	50	67	91	16
No	123	102	77	156

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment-emergent adverse events (TEAEs) during exposure to trial product

End point title	Number of treatment-emergent adverse events (TEAEs) during exposure to trial product
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End point description:

A treatment-emergent adverse event (TEAE) is defined as an adverse event with onset in the on-treatment observation period. This period started at the date of first dose of trial product and included the period after initiation of rescue medication, if any, and excluded the period after premature trial

product discontinuation, if any. The safety analysis set (SAS) comprised all randomised subjects who received at least one dose of trial product. Subjects contribute to a treatment group based on the trial product they actually received for the majority of the on-treatment observation period. "Number of subjects analysed" = subjects with available data.

End point type	Secondary
End point timeframe:	
Assessed up to approximately 57 weeks	

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	184	181	181	184
Units: Events	626	555	586	464

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment-emergent severe or blood glucose-confirmed symptomatic hypoglycaemic episodes during exposure to trial product

End point title	Number of treatment-emergent severe or blood glucose-confirmed symptomatic hypoglycaemic episodes during exposure to trial product
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End point description:

Hypoglycaemic episodes defined as treatment-emergent if the onset of the episode occurs within the on-treatment observation period. Severe or BG-confirmed symptomatic hypoglycaemia is an episode that is severe according to the ADA classification or blood glucose-confirmed by a plasma glucose value <3.1 mmol/L (56 mg/dL) with symptoms consistent with hypoglycaemia. The safety analysis set (SAS) comprised all randomised subjects who received at least one dose of trial product. Subjects contribute to a treatment group based on the trial product they actually received for the majority of the on-treatment observation period. "Number of subjects analysed" = subjects with available data.

End point type	Secondary
End point timeframe:	
Assessed up to approximately 57 weeks	

End point values	Oral semaglutide 3 mg	Oral semaglutide 7 mg	Oral semaglutide 14 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	184	181	181	184
Units: Episodes	196	180	147	156

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of first dose of trial product (week 0) to end of treatment (week 52) + 5 weeks of follow-up (until week 57).

Adverse event reporting additional description:

Results are based on the SAS. All presented AEs are TEAEs which were recorded during the exposure to trial products. AEs with onset during the on-treatment observation period were considered treatment-emergent. Number of deaths causally related to treatment is the data considered to present under 'total number of deaths resulting from AEs'.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	Oral Semaglutide 3 mg
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Reporting group description:

Subjects were to take oral semaglutide 3 mg tablets once daily from week 1 to 52.

Reporting group title	Oral Semaglutide 7 mg
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Reporting group description:

Subjects were to take oral semaglutide tablets once daily in a dose escalation manner from week 1 to 52: 3 mg from week 1 to 4 and 7 mg from week 5 to 52.

Reporting group title	Oral Semaglutide 14 mg
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Reporting group description:

Subjects were to take oral semaglutide tablets once daily in a dose escalation manner from week 1 to 52: 3 mg from week 1 to 4, 7 mg from week 5 to 8 and 14 mg from week 9 to 52.

Reporting group title	Placebo
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Reporting group description:

Subjects were to take oral semaglutide placebo tablets once daily from week 1 to 52.

Serious adverse events	Oral Semaglutide 3 mg	Oral Semaglutide 7 mg	Oral Semaglutide 14 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 184 (13.59%)	19 / 181 (10.50%)	12 / 181 (6.63%)
number of deaths (all causes)	0	0	3
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			

subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Prostate cancer			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Rectal adenocarcinoma			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Vulval cancer			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 184 (0.00%)	2 / 181 (1.10%)	0 / 181 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Peripheral artery thrombosis			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Surgical and medical procedures			

Hip arthroplasty			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Hysterectomy			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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 operation			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Thyroidectomy			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Death			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Non-cardiac chest pain			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Oedema peripheral			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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

Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 184 (0.54%)	1 / 181 (0.55%)	0 / 181 (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
Reproductive system and breast disorders			
Prostatomegaly			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal prolapse			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 184 (0.54%)	1 / 181 (0.55%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	1 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Pulmonary oedema			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Respiratory failure			

subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Investigations			
Spinal myelogram			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Jaw fracture			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Joint dislocation			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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

Postoperative thoracic procedure complication			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Rib fracture			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 184 (0.54%)	1 / 181 (0.55%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Angina unstable			
subjects affected / exposed	2 / 184 (1.09%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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

Cardiac failure			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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 failure chronic			
subjects affected / exposed	1 / 184 (0.54%)	1 / 181 (0.55%)	0 / 181 (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
Coronary artery disease			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Myocardial infarction			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Silent myocardial infarction			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Nervous system disorders			
Brain stem infarction			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Carpal tunnel syndrome			

subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemic unconsciousness			
subjects affected / exposed	2 / 184 (1.09%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Ischaemic stroke			
subjects affected / exposed	2 / 184 (1.09%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Mononeuropathy			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
White matter lesion			

subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Normocytic anaemia			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Eye disorders			
Cataract			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Glaucoma			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Retinal detachment			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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

Gastroesophageal reflux disease			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Nausea			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	2 / 181 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	2 / 181 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 184 (0.54%)	1 / 181 (0.55%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical spinal stenosis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Infections and infestations			
Carbuncle			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Diverticulitis			

subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	1 / 181 (0.55%)
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 viral			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected skin ulcer			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Pneumonia pneumococcal			
subjects affected / exposed	0 / 184 (0.00%)	1 / 181 (0.55%)	0 / 181 (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
Postoperative wound infection			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	1 / 181 (0.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 184 (0.54%)	0 / 181 (0.00%)	0 / 181 (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
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			

subjects affected / exposed	0 / 184 (0.00%)	0 / 181 (0.00%)	0 / 181 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 184 (9.24%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal adenocarcinoma			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vulval cancer			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic stenosis			

subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral artery thrombosis			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Hip arthroplasty			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hysterectomy			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal operation			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thyroidectomy			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Prostatomegaly			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine polyp			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vaginal prolapse			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression suicidal			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Spinal myelogram			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Clavicle fracture			

subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Jaw fracture			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Postoperative thoracic procedure complication			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial flutter			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure chronic			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery stenosis			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			

subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Silent myocardial infarction			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ventricular tachycardia			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Brain stem infarction			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Carpal tunnel syndrome			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral infarction			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemic unconsciousness			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			

subjects affected / exposed	2 / 184 (1.09%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Lacunar infarction			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mononeuropathy			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
White matter lesion			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Normocytic anaemia			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Glaucoma			

subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Retinal detachment			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal inflammation			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Impaired gastric emptying			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			

subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver injury			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cervical spinal stenosis			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			

subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rhabdomyolysis			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Carbuncle			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infected skin ulcer			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia pneumococcal			

subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Postoperative wound infection			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	0 / 184 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 184 (0.54%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Oral Semaglutide 3 mg	Oral Semaglutide 7 mg	Oral Semaglutide 14 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 184 (41.85%)	86 / 181 (47.51%)	100 / 181 (55.25%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 184 (1.63%)	4 / 181 (2.21%)	1 / 181 (0.55%)
occurrences (all)	4	4	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	7 / 184 (3.80%)	11 / 181 (6.08%)	10 / 181 (5.52%)
occurrences (all)	8	12	11
Constipation			

subjects affected / exposed occurrences (all)	8 / 184 (4.35%) 8	15 / 181 (8.29%) 16	12 / 181 (6.63%) 13
Diarrhoea subjects affected / exposed occurrences (all)	16 / 184 (8.70%) 19	22 / 181 (12.15%) 26	26 / 181 (14.36%) 40
Nausea subjects affected / exposed occurrences (all)	21 / 184 (11.41%) 23	30 / 181 (16.57%) 34	41 / 181 (22.65%) 60
Vomiting subjects affected / exposed occurrences (all)	11 / 184 (5.98%) 14	14 / 181 (7.73%) 17	17 / 181 (9.39%) 28
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	27 / 184 (14.67%) 42	21 / 181 (11.60%) 32	18 / 181 (9.94%) 29
Upper respiratory tract infection subjects affected / exposed occurrences (all)	8 / 184 (4.35%) 11	6 / 181 (3.31%) 8	13 / 181 (7.18%) 13
Urinary tract infection subjects affected / exposed occurrences (all)	6 / 184 (3.26%) 10	5 / 181 (2.76%) 6	10 / 181 (5.52%) 10
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	8 / 184 (4.35%) 8	18 / 181 (9.94%) 19	23 / 181 (12.71%) 24

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events subjects affected / exposed	73 / 184 (39.67%)		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	11 / 184 (5.98%) 12		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all)	3 / 184 (1.63%) 3		

Constipation subjects affected / exposed occurrences (all)	5 / 184 (2.72%) 6		
Diarrhoea subjects affected / exposed occurrences (all)	11 / 184 (5.98%) 15		
Nausea subjects affected / exposed occurrences (all)	13 / 184 (7.07%) 19		
Vomiting subjects affected / exposed occurrences (all)	7 / 184 (3.80%) 8		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	27 / 184 (14.67%) 35		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	13 / 184 (7.07%) 17		
Urinary tract infection subjects affected / exposed occurrences (all)	7 / 184 (3.80%) 12		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	2 / 184 (1.09%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 January 2017	New text addressing: 1) Additional eye examinations and additional data collection on diabetic retinopathy. 2) Investigator's responsibility in ensuring evaluation and management of certain risk factors and complications. 3) Clarification of the criteria for completion, withdrawal and lost to follow-up. 4) Week 26 reporting of trial results. 5) Other minor corrections and clarifications
23 June 2017	New text addressing the inclusion in the flow chart of the 7-point SMPG profile at visit 18A, and inclusion of an "Eye Examination Category" in section 17.2 "Definition of analysis sets", and correction of a minor typographical error in section 8.1.5.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported