

**Clinical trial results:****A Randomized, Phase 3, Open-Label Trial Comparing the Effect of LY3298176 versus Titrated Insulin Degludec on Glycemic Control in Patients with Type 2 Diabetes****Summary**

EudraCT number	2018-003422-84
Trial protocol	GR AT HU PL ES IT RO
Global end of trial date	04 January 2021

Results information

Result version number	v1 (current)
This version publication date	18 December 2021
First version publication date	18 December 2021

Trial information**Trial identification**

Sponsor protocol code	I8F-MC-GPGH
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03882970
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16997

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	04 January 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to compare the effect of the study drug tirzepatide to insulin degludec on blood sugar levels in participants with type 2 diabetes. The study will last about 67 weeks and may include up to 22 visits.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 224
Country: Number of subjects enrolled	Austria: 27
Country: Number of subjects enrolled	Greece: 137
Country: Number of subjects enrolled	Hungary: 147
Country: Number of subjects enrolled	Italy: 30
Country: Number of subjects enrolled	Poland: 132
Country: Number of subjects enrolled	Puerto Rico: 35
Country: Number of subjects enrolled	Romania: 214
Country: Number of subjects enrolled	Korea, Republic of: 36
Country: Number of subjects enrolled	Spain: 86
Country: Number of subjects enrolled	Taiwan: 36
Country: Number of subjects enrolled	Ukraine: 45
Country: Number of subjects enrolled	United States: 295
Worldwide total number of subjects	1444
EEA total number of subjects	773

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)	1064
From 65 to 84 years	380
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

No Text Available

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	5 mg Tirzepatide
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Arm description:

5 milligrams (mg) tirzepatide administered subcutaneously (SC) once a week.

Arm type	Experimental
Investigational medicinal product name	Tirzepatide
Investigational medicinal product code	
Other name	LY3298176
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered SC

Arm title	10 mg Tirzepatide
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Arm description:

10 mg tirzepatide administered SC once a week.

Arm type	Experimental
Investigational medicinal product name	Tirzepatide
Investigational medicinal product code	
Other name	LY3298176
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered SC

Arm title	15 mg Tirzepatide
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Arm description:

15 mg tirzepatide administered SC once a week SC.

Arm type	Experimental
Investigational medicinal product name	Tirzepatide
Investigational medicinal product code	
Other name	LY3298176
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered SC

Arm title	Insulin Degludec
Arm description:	
Insulin degludec administered SC once a day. Doses were individualized and titrated according to protocol-defined targets.	
The starting dose of insulin degludec was 10 IU/day ideally at bedtime, titrated to a fasting blood glucose (FBG) <90 milligram per Deciliter (mg/dL), following a treat-to-target (TTT) algorithm based on the last 3 FBG values.	
Arm type	Active comparator
Investigational medicinal product name	Insulin Degludec
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Administered SC	

Number of subjects in period 1	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide
Started	359	361	359
Received at least one dose of study drug	358	360	359
Completed	333	321	340
Not completed	26	40	19
Adverse event, serious fatal	1	2	1
Consent withdrawn by subject	8	17	7
Physician decision	-	2	2
Adverse event, non-fatal	5	7	3
Lost to follow-up	8	9	5
Personal Reason	2	3	1
Protocol deviation	2	-	-

Number of subjects in period 1	Insulin Degludec
Started	365
Received at least one dose of study drug	360
Completed	331
Not completed	34
Adverse event, serious fatal	1
Consent withdrawn by subject	22
Physician decision	2
Adverse event, non-fatal	1
Lost to follow-up	5
Personal Reason	3
Protocol deviation	-

Baseline characteristics

Reporting groups

Reporting group title	5 mg Tirzepatide
Reporting group description: 5 milligrams (mg) tirzepatide administered subcutaneously (SC) once a week.	
Reporting group title	10 mg Tirzepatide
Reporting group description: 10 mg tirzepatide administered SC once a week.	
Reporting group title	15 mg Tirzepatide
Reporting group description: 15 mg tirzepatide administered SC once a week SC.	
Reporting group title	Insulin Degludec
Reporting group description: Insulin degludec administered SC once a day. Doses were individualized and titrated according to protocol-defined targets.	

The starting dose of insulin degludec was 10 IU/day ideally at bedtime, titrated to a fasting blood glucose (FBG) <90 milligram per Deciliter (mg/dL), following a treat-to-target (TTT) algorithm based on the last 3 FBG values.

Reporting group values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide
Number of subjects	359	361	359
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	57.20 ± 10.13	57.40 ± 9.66	57.50 ± 10.24
Gender categorical Units: Subjects			
Female	158	165	165
Male	201	196	194
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	109	108	96
Not Hispanic or Latino	247	253	259
Unknown or Not Reported	3	0	4
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	20	19	20
Native Hawaiian or Other Pacific Islander	1	0	2
Black or African American	13	12	8
White	324	329	327
More than one race	1	0	1
Unknown or Not Reported	0	0	0
Region of Enrollment			

Units: Subjects			
Argentina	57	54	56
Austria	7	8	4
Greece	33	35	35
Hungary	36	37	37
Italy	6	8	8
Poland	33	33	33
Puerto Rico	8	7	11
Romania	54	54	53
South Korea	9	10	8
Spain	21	21	22
Taiwan	9	8	10
Ukraine	11	11	12
United States	75	75	70
Hemoglobin A1c			
Units: Percentage of HbA1c			
arithmetic mean	8.17	8.18	8.21
standard deviation	± 0.89	± 0.89	± 0.94

Reporting group values	Insulin Degludec	Total	
Number of subjects	365	1444	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	57.50		
standard deviation	± 10.08	-	
Gender categorical			
Units: Subjects			
Female	148	636	
Male	217	808	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	108	421	
Not Hispanic or Latino	256	1015	
Unknown or Not Reported	1	8	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	2	4	
Asian	19	78	
Native Hawaiian or Other Pacific Islander	1	4	
Black or African American	11	44	
White	332	1312	
More than one race	0	2	
Unknown or Not Reported	0	0	
Region of Enrollment			
Units: Subjects			
Argentina	57	224	
Austria	8	27	

Greece	34	137	
Hungary	37	147	
Italy	8	30	
Poland	33	132	
Puerto Rico	9	35	
Romania	53	214	
South Korea	9	36	
Spain	22	86	
Taiwan	9	36	
Ukraine	11	45	
United States	75	295	
Hemoglobin A1c			
Units: Percentage of HbA1c			
arithmetic mean	8.12		
standard deviation	± 0.94	-	

End points

End points reporting groups

Reporting group title	5 mg Tirzepatide
Reporting group description:	5 milligrams (mg) tirzepatide administered subcutaneously (SC) once a week.
Reporting group title	10 mg Tirzepatide
Reporting group description:	10 mg tirzepatide administered SC once a week.
Reporting group title	15 mg Tirzepatide
Reporting group description:	15 mg tirzepatide administered SC once a week SC.
Reporting group title	Insulin Degludec
Reporting group description:	Insulin degludec administered SC once a day. Doses were individualized and titrated according to protocol-defined targets.
The starting dose of insulin degludec was 10 IU/day ideally at bedtime, titrated to a fasting blood glucose (FBG) <90 milligram per Deciliter (mg/dL), following a treat-to-target (TTT) algorithm based on the last 3 FBG values.	

Primary: Change from Baseline in Hemoglobin A1c (HbA1c) (10 mg and 15 mg)

End point title	Change from Baseline in Hemoglobin A1c (HbA1c) (10 mg and 15 mg) ^[1]
End point description:	HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time. Least Squares (LS) mean was determined by mixed-model repeated measures (MMRM) model with covariates Baseline + Pooled Country + Baseline Oral Antihyperglycemic Medication (OAM) Use (Metformin (Met), Met plus SGLT-2i) + Treatment + Time + Treatment*Time (Type III sum of squares).
Analysis Population Description: All randomized participants who received at least one dose of study drug and had a baseline and at least 1 post-baseline value, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or stopping study drug (last dose date +7 days).	
End point type	Primary
End point timeframe:	Baseline, Week 52

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Analysis were planned for 10 mg and 15 mg Tirzepatide arms only.

End point values	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Degludec	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	291	294	317	
Units: Percentage of HbA1c				
least squares mean (standard error)	-2.20 (± 0.051)	-2.37 (± 0.050)	-1.34 (± 0.049)	

Statistical analyses

Statistical analysis title	Change from Baseline in Hemoglobin A1c (HbA1c)
Comparison groups	Insulin Degludec v 10 mg Tirzepatide
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[2]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.72

Notes:

[2] - The study was powered for superiority in HbA1c. The sample size provided >99% power to show noninferiority assuming a 0.3% NI boundary, 0.35% greater mean reduction in tirzepatide doses compared to insulin degludec, 1:1:1:1 randomization, a common SD of 1.1%, 1 sided significance level of 0.0125, and a dropout rate of 28%.

Statistical analysis title	Change from Baseline in Hemoglobin A1c (HbA1c)
Comparison groups	15 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	611
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.17
upper limit	-0.9

Notes:

[3] - The study was powered for superiority in HbA1c. The sample size provided >99% power to show noninferiority assuming a 0.3% NI boundary, 0.35% greater mean reduction in tirzepatide doses compared to insulin degludec, 1:1:1:1 randomization, a common SD of 1.1%, 1 sided significance level of 0.0125, and a dropout rate of 28%.

Secondary: Change from Baseline in HbA1c (5 mg)

End point title	Change from Baseline in HbA1c (5 mg) ^[4]
End point description:	
HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time. Least Squares (LS) mean was determined by mixed-model repeated measures (MMRM) model with covariates Baseline + Pooled Country + Baseline OAM Use (Met, Met plus SGLT-2i) + Treatment + Time + Treatment*Time (Type III sum of squares).	
Analysis Population Description: All randomized participants who received at least one dose of study drug and had a baseline and at least 1 post-baseline value, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or stopping study drug (last dose date +7 days).	
End point type	Secondary

End point timeframe:

Baseline, Week 52

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Analysis were planned for 5 mg Tirzepatide arm only.

End point values	5 mg Tirzepatide	Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312	317		
Units: Percentage of HbA1c				
least squares mean (standard error)	-1.93 (± 0.050)	-1.34 (± 0.049)		

Statistical analyses

Statistical analysis title	Change from Baseline in Hemoglobin A1c (HbA1c)
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Statistical analysis description:

The study was powered for superiority in HbA1c. The sample size provided >99% power to show noninferiority assuming a 0.3% NI boundary, 0.35% greater mean reduction in tirzepatide doses compared to insulin degludec, 1:1:1:1 randomization, a common SD of 1.1%, 1 sided significance level of 0.0125, and a dropout rate of 28%.

Comparison groups	5 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	629
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.73
upper limit	-0.45

Secondary: Change from Baseline in Body Weight

End point title	Change from Baseline in Body Weight
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End point description:

LS mean was determined by MMRM model with Baseline + Pooled Country + Baseline OAM Use (Met, Met plus SGLT-2i) + Baseline HbA1c Group (<=8.5%, >8.5%) + Treatment + Time + Treatment*Time (Type III sum of squares) as covariates.

Analysis Population Description: All randomized participants who received at least one dose of study drug and had a baseline and at least 1 post-baseline value, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or stopping study drug (last dose date +7 days).

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Degludec
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	310	291	295	317
Units: Kilograms (kg)				
least squares mean (standard error)	-7.5 (\pm 0.37)	-10.7 (\pm 0.37)	-12.9 (\pm 0.37)	2.3 (\pm 0.37)

Statistical analyses

Statistical analysis title	Change from Baseline in Body Weight
Comparison groups	5 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	627
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-9.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.8
upper limit	-8.8

Statistical analysis title	Change from Baseline in Body Weight
Comparison groups	10 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14
upper limit	-11.9

Statistical analysis title	Change from Baseline in Body Weight
Comparison groups	15 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	612
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-15.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.2
upper limit	-14.2

Secondary: Change from Baseline in Fasting Serum Glucose

End point title	Change from Baseline in Fasting Serum Glucose
End point description:	
LS mean was determined by MMRM model with variables Baseline + Pooled Country + Baseline OAM Use (Met, Met plus SGLT-2i) + Baseline HbA1c Group ($\leq 8.5\%$, $> 8.5\%$) + Treatment + Time + Treatment*Time (Type III sum of squares).	
Analysis Population Description: All randomized participants who received at least one dose of study drug and had a baseline and at least 1 post-baseline value, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or stopping study drug (last dose date +7 days).	
End point type	Secondary
End point timeframe:	
Baseline, Week 52	

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Degludec
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	309	291	293	314
Units: milligram per Deciliter (mg/dL)				
least squares mean (standard error)	-48.2 (\pm 1.82)	-54.8 (\pm 1.86)	-59.2 (\pm 1.85)	-55.7 (\pm 1.81)

Statistical analyses

Statistical analysis title	Change from Baseline in Fasting Serum Glucose
Comparison groups	5 mg Tirzepatide v Insulin Degludec

Number of subjects included in analysis	623
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	12.5

Statistical analysis title	Change from Baseline in Fasting Serum Glucose
Comparison groups	10 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	605
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.751
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	5.9

Statistical analysis title	Change from Baseline in Fasting Serum Glucose
Comparison groups	15 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	607
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.168
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.7
upper limit	1.5

Secondary: Percentage of Participants Achieving an HbA1cTarget Value of <7%

End point title	Percentage of Participants Achieving an HbA1c Target Value of <7%
End point description:	
Hemoglobin A1c (HbA1c) is the glycosylated fraction of hemoglobin A. HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time. Imputed data includes observed value and imputed value if endpoint measure is missing. Missing endpoint measures are imputed by predictions from an MMRM analysis model using observed data in the efficacy analysis set and adjusted for Baseline Value, Pooled Country, Baseline OAM Use (Met, Met plus SGLT-2i), Treatment, Visit and Visit*Treatment.	
Analysis Population Description: All randomized participants who received at least one dose of study drug and had a baseline and at least 1 post-baseline value, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or stopping study drug (last dose date +7 days).	
End point type	Secondary
End point timeframe:	
Week 52	

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Degludec
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	353	350	353	351
Units: percentage of participants				
number (not applicable)	82.44	89.71	92.63	61.25

Statistical analyses

Statistical analysis title	Participants Achieving HbA1c Target Value of <7%
Comparison groups	5 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.38
upper limit	5.01

Statistical analysis title	Participants Achieving HbA1c Target Value of <7%
Comparison groups	Insulin Degludec v 10 mg Tirzepatide

Number of subjects included in analysis	701
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.55
upper limit	10.84

Statistical analysis title	Participants Achieving HbA1c Target Value of <7%
Comparison groups	15 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	10.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.65
upper limit	17.48

Secondary: Mean Change From Baseline in Daily Average 7-Point Self-Monitored Blood Glucose (SMBG) Values

End point title	Mean Change From Baseline in Daily Average 7-Point Self-Monitored Blood Glucose (SMBG) Values
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End point description:

The self-monitored plasma glucose (SMBG) data were collected at the following 7 time points: Morning Premeal - Fasting, Morning 2-hour Postmeal, Midday Premeal, Midday 2-hour Postmeal, Evening Premeal, Evening 2-hour Postmeal and Bedtime. LS mean was determined by mixed-model repeated measures (MMRM) model with variables Baseline + Baseline HbA1c Group ($\leq 8.5\%$, $> 8.5\%$) + Pooled Country + Baseline OAM Use (Met, Met plus SGLT-2i) + Treatment + Time + Treatment*Time (Type III sum of squares).

Analysis Population Description: All randomized participants who received at least one dose of study drug and had a baseline and at least 1 post-baseline value, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or stopping study drug (last dose date +7 days).

End point type	Secondary
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End point timeframe:

Baseline, Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Degludec
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	281	263	274	288
Units: mg/dL				
least squares mean (standard error)	-52.6 (± 1.20)	-59.7 (± 1.22)	-60.6 (± 1.20)	-48.0 (± 1.18)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved WeightLoss ≥5%

End point title	Percentage of Participants who Achieved WeightLoss ≥5%
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End point description:

Percentage of Participants who Achieved Weight Loss ≥5%

Analysis Population Description: All randomized participants who received at least one dose of study drug and had a baseline and at least 1 post-baseline value, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or stopping study drug (last dose date +7 days).

End point type	Secondary
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End point timeframe:

Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Degludec
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	353	350	353	351
Units: percentage of participants				
number (not applicable)	66.01	83.71	87.82	6.27

Statistical analyses

Statistical analysis title	Percentage Participants who Achieved WeightLoss ≥5
Comparison groups	Insulin Degludec v 5 mg Tirzepatide
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	29.78

Confidence interval	
level	95 %
sides	2-sided
lower limit	18.35
upper limit	48.35

Statistical analysis title	Percentage Participants who Achieved WeightLoss ≥ 5
Comparison groups	10 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	701
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	79.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	47.56
upper limit	134.17

Statistical analysis title	Percentage Participants who Achieved WeightLoss ≥ 5
Comparison groups	15 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	704
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	110.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	64.73
upper limit	189.55

Secondary: Diabetes Treatment Satisfaction as measured by the Diabetes Treatment Satisfaction Questionnaire, change version (DTSQc) Hyperglycemia, Hypoglycemia and Total Score

End point title	Diabetes Treatment Satisfaction as measured by the Diabetes Treatment Satisfaction Questionnaire, change version (DTSQc) Hyperglycemia, Hypoglycemia and Total Score
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End point description:

DTSQc, an 8-item questionnaire, assesses relative change in treatment satisfaction perceived frequency of hyperglycemia, and perceived frequency of hypoglycemia from baseline to week 52 or early

termination. The treatment satisfaction score ranges from -18 to 18 where the higher the score the greater the improvement in satisfaction with treatment. The lower the score the greater the deterioration in satisfaction with treatment. The hyperglycemia and hypoglycemia scores range from -3 to 3 where negative scores indicate fewer problems with blood glucose levels and positive scores indicate more problems than before. LS mean was determined by ANCOVA model for endpoint measures: Variable = Baseline DTSQs + Pooled Country + Baseline HbA1c Group ($\leq 8.5\%$, $> 8.5\%$) + Baseline OAM Use (Met, Met plus SGLT-2i) + Treatment (Type III sum of squares).

End point type	Secondary
End point timeframe:	
Week 52	

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Degludec
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	306	293	292	313
Units: units on a scale				
least squares mean (standard error)				
Hyperglycemia	-1.4 (± 0.11)	-1.4 (± 0.11)	-1.6 (± 0.11)	-1.1 (± 0.11)
Hypoglycemia	-1.1 (± 0.12)	-0.9 (± 0.12)	-1.0 (± 0.12)	-0.7 (± 0.12)
Total Score	15.6 (± 0.27)	15.5 (± 0.28)	15.6 (± 0.28)	12.6 (± 0.27)

Statistical analyses

Statistical analysis title	Hyperglycemia (5 mg Tirzepatide, Insulin Degludec)
Statistical analysis description:	
Hyperglycemia	
Comparison groups	5 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	619
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.096
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.05

Statistical analysis title	Hyperglycemia (10mg Tirzepatide, Insulin Degludec)
Statistical analysis description:	
Hyperglycemia	
Comparison groups	Insulin Degludec v 10 mg Tirzepatide

Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.113
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.06

Statistical analysis title	Hyperglycemia (15 mg Tirzepatide, Insulin Degludec)
Statistical analysis description: Hyperglycemia	
Comparison groups	15 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	605
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.78
upper limit	-0.16

Statistical analysis title	Hypoglycemia (5 mg Tirzepatide, Insulin Degludec)
Statistical analysis description: Hypoglycemia	
Comparison groups	5 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	619
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.74
upper limit	-0.08

Statistical analysis title	Hypoglycemia (10 mg Tirzepatide, Insulin Degludec)
Statistical analysis description:	
Hypoglycemia	
Comparison groups	10 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.28
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	0.15

Statistical analysis title	Hypoglycemia (15 mg Tirzepatide, Insulin Degludec)
Statistical analysis description:	
Hypoglycemia	
Comparison groups	15 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	605
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.129
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	0.07

Statistical analysis title	Total Score (5 mg Tirzepatide, Insulin Degludec)
Statistical analysis description:	
Total Score	
Comparison groups	5 mg Tirzepatide v Insulin Degludec

Number of subjects included in analysis	619
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.26
upper limit	3.75

Statistical analysis title	Total Score (10 mg Tirzepatide, Insulin Degludec)
Statistical analysis description:	
Total Score	
Comparison groups	10 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.15
upper limit	3.65

Statistical analysis title	Total Score (15 mg Tirzepatide, Insulin Degludec)
Statistical analysis description:	
Total Score	
Comparison groups	15 mg Tirzepatide v Insulin Degludec
Number of subjects included in analysis	605
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.24
upper limit	3.74

Secondary: Rate of Hypoglycemia with Blood Glucose <54 milligram/deciliter (mg/dL) [<3.0 (millimole/liter (mmol/L))] or Severe Hypoglycemia

End point title	Rate of Hypoglycemia with Blood Glucose <54 milligram/deciliter (mg/dL) [<3.0 (millimole/liter (mmol/L))] or Severe Hypoglycemia
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End point description:

Hypoglycemia events were defined by participant reported events with blood glucose<54mg/dL (<3.0 mmol/L) or severe hypoglycemia. Severe hypoglycemia is defined as an episode with severe cognitive impairment requiring the assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions. These episodes may be associated with sufficient neuroglycopenia to induce seizure or coma. The rate of postbaseline hypoglycemia was estimated by negative binomial model: Number of episodes = Pooled Country+Baseline OAM Use (Met, Met plus SGLT-2i)+Baseline HbA1c Group (<=8.5%, >8.5%)+Treatment, with log (exposure in days/365.25) as an offset variable.

Randomized participants who received at least one dose of study drug and had a baseline and at least 1 post-baseline value, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or stopping study drug (last dose data + 7 days).

End point type	Secondary
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End point timeframe:

Baseline through Safety Follow-Up (Up to Week 56)

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Degludec
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	356	360	359	358
Units: Episodes/participant/365.25 days				
arithmetic mean (standard error)	0.0137 (± 0.0056)	0.0108 (± 0.0044)	0.0275 (± 0.0143)	0.1020 (± 0.0568)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline Up To 56 Weeks

Adverse event reporting additional description:

All participants who received at least one dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	5 mg Tirzepatide
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Reporting group description:

5 milligrams (mg) tirzepatide administered subcutaneously (SC) once a week.

Reporting group title	10 mg Tirzepatide
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Reporting group description:

5 milligrams (mg) tirzepatide administered subcutaneously (SC) once a week.

Reporting group title	15 mg Tirzepatide
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Reporting group description:

15 mg tirzepatide administered SC once a week SC.

Reporting group title	Insulin Degludec
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Reporting group description:

Insulin degludec administered SC once a day. Doses were individualized and titrated according to protocol-defined targets.

The starting dose of insulin degludec was 10 IU/day ideally at bedtime, titrated to a fasting blood glucose (FBG) <90 milligram per Deciliter (mg/dL), following a treat-to-target (TTT) algorithm based on the last 3 FBG values.

Serious adverse events	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 358 (8.10%)	20 / 360 (5.56%)	26 / 359 (7.24%)
number of deaths (all causes)	1	2	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenocarcinoma of colon			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholangiocarcinoma			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
gastric neoplasm alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
invasive breast carcinoma alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
invasive ductal breast carcinoma alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
lung adenocarcinoma stage iv alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
metastases to liver alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
neoplasm skin alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

neuroendocrine carcinoma alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pituitary tumour benign alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
squamous cell carcinoma alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
testicular neoplasm alternative dictionary used: MedDRA 23.1			
subjects affected / exposed ^[1]	1 / 200 (0.50%)	0 / 195 (0.00%)	0 / 194 (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
transitional cell carcinoma alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
Vascular disorders			
deep vein thrombosis alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
dry gangrene alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
abortion spontaneous			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed ^[2]	0 / 158 (0.00%)	1 / 165 (0.61%)	0 / 165 (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
General disorders and administration site conditions			
multiple organ dysfunction syndrome			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
necrosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
non-cardiac chest pain			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	2 / 358 (0.56%)	0 / 360 (0.00%)	0 / 359 (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
Reproductive system and breast disorders			
cervical dysplasia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed ^[3]	0 / 158 (0.00%)	0 / 165 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

asthma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumothorax			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
pulmonary embolism			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
respiratory failure			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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			
alcohol abuse			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
depression suicidal			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
major depression			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
suicide attempt			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
Investigations			
sars-cov-2 test positive			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
Injury, poisoning and procedural complications			
accident			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
ankle fracture			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
craniocerebral injury			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
femur fracture			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
foot fracture alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
head injury alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hip fracture alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
injury alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
limb traumatic amputation alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
lumbar vertebral fracture alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

maternal exposure during pregnancy			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed ^[4]	0 / 158 (0.00%)	1 / 165 (0.61%)	0 / 165 (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
tendon injury			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
Congenital, familial and genetic disorders			
arrhythmogenic right ventricular dysplasia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	2 / 358 (0.56%)	0 / 360 (0.00%)	0 / 359 (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
atrial fibrillation			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
atrial tachycardia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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 arrest			

alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
cardiac failure			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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 congestive			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
cardio-respiratory arrest			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
coronary artery disease			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	1 / 360 (0.28%)	0 / 359 (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
myocardial infarction			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	1 / 360 (0.28%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ventricular tachycardia			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
diabetic neuropathy			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
haemorrhagic stroke			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
subarachnoid haemorrhage			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
syncope			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	2 / 358 (0.56%)	0 / 360 (0.00%)	0 / 359 (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
vertebrobasilar insufficiency alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
Blood and lymphatic system disorders neutropenia alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
thrombocytopenia alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
Ear and labyrinth disorders vertigo alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
Eye disorders cataract alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
retinal detachment alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
diarrhoea			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
diverticulum intestinal haemorrhagic			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
dyspepsia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
gastric ulcer haemorrhage			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
gastritis alcoholic			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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 haemorrhage alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
inguinal hernia alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
lower gastrointestinal haemorrhage alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
pancreatitis acute alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
segmental diverticular colitis alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
Hepatobiliary disorders cholecystitis alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholelithiasis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	1 / 360 (0.28%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
malignant biliary obstruction			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
diabetic foot			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
skin ulcer			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
haematuria			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
nephrolithiasis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	1 / 360 (0.28%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal colic			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	1 / 360 (0.28%)	0 / 359 (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
Endocrine disorders			
inappropriate antidiuretic hormone secretion			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
lumbar spinal stenosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
rotator cuff syndrome			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
Infections and infestations			
covid-19			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
covid-19 pneumonia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	1 / 360 (0.28%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
cellulitis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
cellulitis orbital			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
colon gangrene			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
coronavirus infection			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
device related infection alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diverticulitis alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
endocarditis alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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
gastroenteritis alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	1 / 360 (0.28%)	1 / 359 (0.28%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hepatitis e alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 358 (0.28%)	0 / 360 (0.00%)	0 / 359 (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
intervertebral discitis alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 358 (0.00%)	0 / 360 (0.00%)	0 / 359 (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

osteomyelitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 358 (0.00%) 0 / 0 0 / 0	1 / 360 (0.28%) 0 / 1 0 / 0	0 / 359 (0.00%) 0 / 0 0 / 0
pneumonia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 358 (0.00%) 0 / 0 0 / 0	0 / 360 (0.00%) 0 / 0 0 / 0	2 / 359 (0.56%) 0 / 2 0 / 0
pyelonephritis acute alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 358 (0.00%) 0 / 0 0 / 0	0 / 360 (0.00%) 0 / 0 0 / 0	1 / 359 (0.28%) 0 / 1 0 / 0
sepsis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 358 (0.00%) 0 / 0 0 / 0	0 / 360 (0.00%) 0 / 0 0 / 0	1 / 359 (0.28%) 0 / 1 0 / 0
septic shock alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 358 (0.00%) 0 / 0 0 / 0	0 / 360 (0.00%) 0 / 0 0 / 0	0 / 359 (0.00%) 0 / 0 0 / 0
systemic candida alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 358 (0.00%) 0 / 0 0 / 0	0 / 360 (0.00%) 0 / 0 0 / 0	0 / 359 (0.00%) 0 / 0 0 / 0

Serious adverse events	Insulin Degludec		
Total subjects affected by serious adverse events			

subjects affected / exposed	22 / 360 (6.11%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenocarcinoma of colon			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
cholangiocarcinoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
gastric neoplasm			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
invasive breast carcinoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
invasive ductal breast carcinoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
lung adenocarcinoma stage iv			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
metastases to liver				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
neoplasm skin				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
neuroendocrine carcinoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pituitary tumour benign				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
squamous cell carcinoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
testicular neoplasm				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed ^[1]	0 / 213 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

transitional cell carcinoma alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 360 (0.28%) 0 / 1 0 / 0		
Vascular disorders deep vein thrombosis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
dry gangrene alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
Pregnancy, puerperium and perinatal conditions abortion spontaneous alternative dictionary used: MedDRA 23.1 subjects affected / exposed ^[2] occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 147 (0.00%) 0 / 0 0 / 0		
General disorders and administration site conditions multiple organ dysfunction syndrome alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all necrosis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 360 (0.28%) 0 / 1 0 / 1 0 / 360 (0.00%) 0 / 0 0 / 0		

non-cardiac chest pain alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
Reproductive system and breast disorders cervical dysplasia alternative dictionary used: MedDRA 23.1 subjects affected / exposed ^[3] occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 147 (0.00%) 0 / 0 0 / 0		
Respiratory, thoracic and mediastinal disorders asthma alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
pneumothorax alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
pulmonary embolism alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 360 (0.28%) 0 / 1 0 / 0		
respiratory failure alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
Psychiatric disorders			

alcohol abuse alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 360 (0.28%) 0 / 1 0 / 0		
depression suicidal alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
major depression alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
suicide attempt alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 360 (0.28%) 0 / 2 0 / 0		
Investigations sars-cov-2 test positive alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
Injury, poisoning and procedural complications accident alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all ankle fracture	0 / 360 (0.00%) 0 / 0 0 / 0		

alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
craniocerebral injury				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
femur fracture				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
foot fracture				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
head injury				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hip fracture				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
injury				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
limb traumatic amputation alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
lumbar vertebral fracture alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
maternal exposure during pregnancy alternative dictionary used: MedDRA 23.1			
subjects affected / exposed ^[4]	0 / 147 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
tendon injury alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
arrhythmogenic right ventricular dysplasia alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
acute myocardial infarction alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	2 / 360 (0.56%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
atrial fibrillation				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
atrial tachycardia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cardiac arrest				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cardiac failure				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 360 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
cardiac failure congestive				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 360 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
cardio-respiratory arrest				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

coronary artery disease alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 360 (0.28%) 0 / 1 0 / 0			
myocardial infarction alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0			
ventricular tachycardia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0			
Nervous system disorders diabetic neuropathy alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 360 (0.28%) 0 / 1 0 / 0			
haemorrhagic stroke alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 360 (0.28%) 0 / 1 0 / 0			
hypoglycaemic unconsciousness alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0			
subarachnoid haemorrhage alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
syncope			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
transient ischaemic attack			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
vertebrobasilar insufficiency			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
neutropenia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
thrombocytopenia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
cataract			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
retinal detachment			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
diarrhoea			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
diverticulum intestinal haemorrhagic			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
dyspepsia			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastric ulcer haemorrhage				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastritis alcoholic				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastrointestinal haemorrhage				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
inguinal hernia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lower gastrointestinal haemorrhage				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pancreatitis acute				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

segmental diverticular colitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
Hepatobiliary disorders cholecystitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
cholelithiasis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
malignant biliary obstruction alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
Skin and subcutaneous tissue disorders diabetic foot alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 360 (0.00%) 0 / 0 0 / 0		
skin ulcer alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 360 (0.28%) 0 / 1 0 / 0		
Renal and urinary disorders acute kidney injury			

alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
haematuria			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
nephrolithiasis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
renal colic			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
inappropriate antidiuretic hormone secretion			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
lumbar spinal stenosis			
alternative dictionary used:			

MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
rotator cuff syndrome			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
covid-19			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
covid-19 pneumonia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
cellulitis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 360 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
cellulitis orbital			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
colon gangrene			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	1 / 360 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
coronavirus infection				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
device related infection				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
diverticulitis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 360 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
endocarditis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 360 (0.28%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
gastroenteritis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hepatitis e				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 360 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

intervertebral discitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 360 (0.28%) 0 / 1 0 / 0			
osteomyelitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 360 (0.28%) 0 / 1 0 / 0			
pneumonia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 2 / 360 (0.56%) 0 / 2 0 / 0			
pyelonephritis acute alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 360 (0.00%) 0 / 0 0 / 0			
sepsis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 360 (0.00%) 0 / 0 0 / 0			
septic shock alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 360 (0.28%) 0 / 1 0 / 0			
systemic candida alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	1 / 360 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly

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

Non-serious adverse events	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide
Total subjects affected by non-serious adverse events			
subjects affected / exposed	124 / 358 (34.64%)	157 / 360 (43.61%)	179 / 359 (49.86%)
Investigations			
lipase increased			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	21 / 358 (5.87%)	16 / 360 (4.44%)	20 / 359 (5.57%)
occurrences (all)	25	18	21
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	11 / 358 (3.07%)	7 / 360 (1.94%)	11 / 359 (3.06%)
occurrences (all)	11	8	11
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	7 / 358 (1.96%)	17 / 360 (4.72%)	23 / 359 (6.41%)
occurrences (all)	7	28	46
diarrhoea			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	55 / 358 (15.36%)	59 / 360 (16.39%)	56 / 359 (15.60%)
occurrences (all)	92	97	107

dyspepsia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences (all)	14 / 358 (3.91%) 14	32 / 360 (8.89%) 39	18 / 359 (5.01%) 28
nausea alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences (all)	41 / 358 (11.45%) 86	81 / 360 (22.50%) 140	85 / 359 (23.68%) 240
vomiting alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences (all)	21 / 358 (5.87%) 29	34 / 360 (9.44%) 53	36 / 359 (10.03%) 63
Infections and infestations nasopharyngitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences (all)	11 / 358 (3.07%) 11	14 / 360 (3.89%) 15	15 / 359 (4.18%) 16
Metabolism and nutrition disorders decreased appetite alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences (all)	22 / 358 (6.15%) 23	37 / 360 (10.28%) 59	43 / 359 (11.98%) 54

Non-serious adverse events	Insulin Degludec		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 360 (18.33%)		
Investigations lipase increased alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences (all)	7 / 360 (1.94%) 7		
Vascular disorders hypertension alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences (all)	21 / 360 (5.83%) 22		
Gastrointestinal disorders			

<p>abdominal pain</p> <p>alternative dictionary used: MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 360 (1.11%)</p> <p>5</p>		
<p>diarrhoea</p> <p>alternative dictionary used: MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>14 / 360 (3.89%)</p> <p>18</p>		
<p>dyspepsia</p> <p>alternative dictionary used: MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 360 (0.00%)</p> <p>0</p>		
<p>nausea</p> <p>alternative dictionary used: MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>6 / 360 (1.67%)</p> <p>6</p>		
<p>vomiting</p> <p>alternative dictionary used: MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 360 (1.11%)</p> <p>4</p>		
<p>Infections and infestations</p> <p>nasopharyngitis</p> <p>alternative dictionary used: MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>22 / 360 (6.11%)</p> <p>27</p>		
<p>Metabolism and nutrition disorders</p> <p>decreased appetite</p> <p>alternative dictionary used: MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 360 (0.56%)</p> <p>2</p>		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 July 2020	Mobile visits may be performed at patients' homes when patients cannot travel to the site due to extenuating circumstances. This provides an option to conduct a clinical trial visit and all the applicable procedures in a mobile healthcare facility or at the home of a patient when the patient is not able or not willing to go to the site due to COVID-19 restrictions.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported