Clinical trial results:
A Randomized, Phase 3, Open-label Trial Comparing the Effect of the Addition of Tirzepatide Once Weekly versus Insulin Lispro (U100) Three Times Daily in Participants with Type 2 Diabetes Inadequately Controlled on Insulin Glargine (U100) with or without Metformin

Summary

EudraCT number	2020-000284-23
Trial protocol	DE HU CZ SK GR IT
Global end of trial date	01 November 2022

Results information

Result version number	v1 (current)
This version publication date	26 October 2023
First version publication date	26 October 2023

Trial information

Trial identification

Sponsor protocol code	I8F-MC-GPHD

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04537923
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17204

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	01 November 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 November 2022
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 safety and efficacy of the study drug tirzepatide to insulin lispro (U100) three times a day in participants with type 2 diabetes that are already on insulin glargine (U100), with or without metformin.

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	19 October 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 417
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Brazil: 281
Country: Number of subjects enrolled	Czechia: 57
Country: Number of subjects enrolled	Germany: 47
Country: Number of subjects enrolled	Greece: 15
Country: Number of subjects enrolled	Hungary: 19
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Mexico: 118
Country: Number of subjects enrolled	Romania: 78
Country: Number of subjects enrolled	Russian Federation: 107
Country: Number of subjects enrolled	Slovakia: 83
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	Turkey: 4
Country: Number of subjects enrolled	United States: 169
Worldwide total number of subjects	1428
EEA total number of subjects	332

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)	980
From 65 to 84 years	445
85 years and over	3

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
Arm title	5 mg Tirzepatide

Arm description:

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

Arm type	Experimental
Investigational medicinal product name	Tirzepatide 5 mg
Investigational medicinal product code	
Other name	LY3298176
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Tirzepatide administered SC once a week.

Arm title	10 mg Tirzepatide

Arm description:

Participants received 10 mg tirzepatide administered SC once a week.

Arm type	Experimental
Investigational medicinal product name	Tirzepatide 10 mg
Investigational medicinal product code	
Other name	LY3298176
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Tirzepatide administered SC once a week.

Arm title	15 mg Tirzepatide

Arm description:

Participants received 15 mg tirzepatide administered SC once a week.

Arm type	Experimental
Investigational medicinal product name	Tirzepatide 15 mg
Investigational medicinal product code	
Other name	LY3298176
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Tirzepatide administered SC once a week.

Arm title	Insulin Lispro

Arm description:

Participants received Insulin lispro 100 units per milliliter (U100) administered SC three times a day.

Arm type	Active comparator
Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	Humalog
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin Lispro 100 units per milliliter (U100) administered SC three times a day.

Number of subjects in period 1	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide
Started	243	238	236
Received at Least One Dose of Study Drug	243	238	225
Completed	228	228	225
Not completed	15	10	11
Missed study visits	2	-	-
Sponsor's decision	-	-	1
Consent withdrawn by subject	4	4	4
Safety reasons	1	-	-
Physician decision	1	-	2
Adverse event, non-fatal	2	1	2
Death	3	3	1
Pregnancy	1	-	-
Lost to follow-up	1	2	1

Number of subjects in period 1	Insulin Lispro
Started	711
Received at Least One Dose of Study Drug	708
Completed	623
Not completed	88
Missed study visits	3
Sponsor's decision	1
Consent withdrawn by subject	58
Safety reasons	-
Physician decision	5
Adverse event, non-fatal	4
Death	11
Pregnancy	-

Lost to follow-up	6

Baseline characteristics

Reporting groups	
Reporting group title	5 mg Tirzepatide
Reporting group description:	
Participants received 5 milligrams (mg) tirzepatide administered subcutaneously (SC) once a week.	
Reporting group title	10 mg Tirzepatide
Reporting group description:	
Participants received 10 mg tirzepatide administered SC once a week.	
Reporting group title	15 mg Tirzepatide
Reporting group description:	
Participants received 15 mg tirzepatide administered SC once a week.	
Reporting group title	Insulin Lispro
Reporting group description:	
Participants received Insulin lispro 100 units per milliliter (U100) administered SC three times a day.	

Reporting group values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide
Number of subjects	243	238	236
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	58.0	59.6	58.2
standard deviation	± 10.2	± 9.4	± 9.6
Gender categorical Units: Subjects			
Female	144	149	133
Male	99	89	103
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	148	142	149
Not Hispanic or Latino	95	93	87
Unknown or Not Reported	0	3	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	2	0	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	11	9	11
White	230	224	220
More than one race	0	5	2
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Argentina	70	70	70
Belgium	0	1	0
Brazil	47	47	46

Czechia	10	9	9
Germany	7	8	8
Greece	2	2	2
Hungary	4	4	2
Italy	1	2	1
Mexico	19	20	20
Romania	14	14	12
Russia	19	17	19
Slovakia	16	13	15
Spain	5	3	3
Turkey	1	0	1
United States	28	28	28
Hemoglobin A1c			
HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time.			
Units: Percentage of HbA1c			
arithmetic mean	8.89	8.78	8.74
standard deviation	± 0.97	± 0.98	± 1.01

Reporting group values	Insulin Lispro	Total	
Number of subjects	711	1428	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	59.00		
standard deviation	± 9.74	-	
Gender categorical			
Units: Subjects			
Female	398	824	
Male	313	604	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	446	885	
Not Hispanic or Latino	261	536	
Unknown or Not Reported	4	7	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	2	3	
Asian	4	8	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	26	57	
White	671	1345	
More than one race	8	15	
Unknown or Not Reported	0	0	
Region of Enrollment			
Units: Subjects			
Argentina	207	417	
Belgium	1	2	
Brazil	141	281	

Czechia	29	57	
Germany	24	47	
Greece	9	15	
Hungary	9	19	
Italy	2	6	
Mexico	59	118	
Romania	38	78	
Russia	52	107	
Slovakia	39	83	
Spain	14	25	
Turkey	2	4	
United States	85	169	
Hemoglobin A1c			
HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured primarily to identify average plasma glucose concentration over prolonged periods of time.			
Units: Percentage of HbA1c			
arithmetic mean	8.81		
standard deviation	± 0.96	-	

End points

End points reporting groups

Reporting group title	5 mg Tirzepatide
Reporting group description:	
Participants received 5 milligrams (mg) tirzepatide administered subcutaneously (SC) once a week.	
Reporting group title	10 mg Tirzepatide
Reporting group description:	
Participants received 10 mg tirzepatide administered SC once a week.	
Reporting group title	15 mg Tirzepatide
Reporting group description:	
Participants received 15 mg tirzepatide administered SC once a week.	
Reporting group title	Insulin Lispro
Reporting group description:	
Participants received Insulin lispro 100 units per milliliter (U100) administered SC three times a day.	
Subject analysis set title	Pooled 5 mg/10 mg/15 mg Tirzepatide
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received either 5 mg or 10 mg or 15 mg tirzepatide administered SC once a week.	

Primary: Change from Baseline in Hemoglobin A1c (HbA1c) (Pooled Doses of Tirzepatide 5 mg, 10 mg and 15 mg)

End point title	Change from Baseline in Hemoglobin A1c (HbA1c) (Pooled Doses of Tirzepatide 5 mg, 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 Metformin Use (Yes, No) + Treatment + Time + Treatment*Time (Type III sum of squares). Analysis Population Description (APD): All randomly assigned participants who took at least 1 dose of study drug and had a baseline and at least 1 post-baseline value for this analysis, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or prematurely stopping study drug. This analysis was planned to measure the outcome for pooled 5 mg, 10 mg and 15 mg tirzepatide.

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: As per planned analysis, the endpoint was assessed for Pooled Doses of Tirzepatide 5 mg, 10 mg and 15 mg.

End point values	Insulin Lispro	Pooled 5 mg/10 mg/15 mg Tirzepatide		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	692	708		
Units: Percentage of HbA1c				
least squares mean (standard error)	-1.16 (± 0.049)	-2.26 (± 0.048)		

Statistical analyses

Statistical analysis title	Outcome measure 1
Comparison groups	Insulin Lispro v Pooled 5 mg/10 mg/15 mg Tirzepatide
Number of subjects included in analysis	1400
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	-0.97

Notes:

[2] - 0.3% noninferiority margin.

Secondary: Change from Baseline in HbA1c

End point title	Change from Baseline in HbA1c

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. LS mean was determined by MMRM model with covariates Baseline + Pooled Country + Baseline Metformin Use (Yes, No) + Treatment + Time + Treatment*Time (Type III sum of squares). APD: All randomly assigned participants who took at least 1 dose of study drug and had a baseline and at least 1 post-baseline value for this analysis, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or prematurely stopping study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Lispro
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	241	234	233	692
Units: Percentage of HbA1c				
least squares mean (standard error)	-2.05 (± 0.082)	-2.27 (± 0.083)	-2.46 (± 0.084)	-1.16 (± 0.049)

Statistical analyses

Statistical analysis title	Outcome measure 2
Comparison groups	5 mg Tirzepatide v Insulin Lispro

Number of subjects included in analysis	933
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.08
upper limit	-0.7

Notes:

[3] - 0.3% noninferiority margin.

Statistical analysis title	Outcome measure 2
Comparison groups	10 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	926
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.92

Notes:

[4] - 0.3% noninferiority margin.

Statistical analysis title	Outcome measure 2
Comparison groups	15 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	925
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.49
upper limit	-1.11

Notes:

[5] - 0.3% noninferiority margin.

Secondary: Percentage of Participants with HbA1c Target Values <7.0%

End point title	Percentage of Participants with HbA1c Target Values <7.0%

End point description:

HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time. APD: All randomly assigned participants who took at least 1 dose of study drug and had a baseline and at least 1 post-baseline value for this analysis, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or prematurely stopping study drug.

End point type	Secondary

End point timeframe:

Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Lispro
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	242	238	236	708
Units: Percentage of participants				
number (not applicable)	61.04	75.64	79.86	36.69

Statistical analyses

Statistical analysis title	Outcome measure 3
Comparison groups	5 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	950
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.25
upper limit	4.36

Statistical analysis title	Outcome measure 3
Comparison groups	10 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	946
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	6.16

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.27
upper limit	8.88

Statistical analysis title	Outcome measure 3
Comparison groups	15 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	944
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.37
upper limit	11.75

Secondary: Change from Baseline in Body Weight

End point title	Change from Baseline in Body Weight

End point description:

LS mean was determined by MMRM model with Baseline + Pooled Country + Baseline Metformin Use (Yes, No) + Baseline HbA1c Group (<=8.5%, >8.5%) + Treatment + Time + Treatment*Time (Type III sum of squares). APD: All randomly assigned participants who took at least 1 dose of study drug and had a baseline and at least 1 post-baseline value for this analysis, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or prematurely stopping study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Lispro
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	241	234	233	694
Units: Kilograms (kg)				
least squares mean (standard error)	-6.9 (± 0.37)	-9.9 (± 0.37)	-12.0 (± 0.38)	3.8 (± 0.22)

Statistical analyses

Statistical analysis title	Outcome measure 4
Comparison groups	5 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	935
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-10.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.5
upper limit	-9.9

Statistical analysis title	Outcome measure 4
Comparison groups	10 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	928
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-13.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.5
upper limit	-12.9

Statistical analysis title	Outcome measure 4
Comparison groups	15 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-15.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.7
upper limit	-15

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 metformin Use (Yes, No) + Baseline HbA1c Group (<=8.5%, >8.5%) + Treatment + Time + Treatment*Time (Type III sum of squares). APD: All randomly assigned participants who took at least 1 dose of study drug and had a baseline and at least 1 post-baseline value for this analysis, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or prematurely stopping study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Lispro
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	241	235	233	694
Units: milligram per Deciliter (mg/dL)				
least squares mean (standard error)	-33.2 (± 3.28)	-43.0 (± 3.32)	-41.6 (± 3.42)	-10.0 (± 1.99)

Statistical analyses

Statistical analysis title	Outcome measure 5
Comparison groups	5 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	935
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-23.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.8
upper limit	-15.7

Statistical analysis title	Outcome measure 5
Comparison groups	10 mg Tirzepatide v Insulin Lispro

Number of subjects included in analysis	929
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.6
upper limit	-25.4

Statistical analysis title	Outcome measure 5
Comparison groups	15 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	927
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-31.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.3
upper limit	-23.8

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

End point title	Change from Baseline in Daily Average 7-Point Self-Monitored Blood Glucose (SMBG) Values

End point description:

The self-monitored plasma glucose (SMBG) data were collected at the following 7 time points: Morning Premeal - Fasting, Morning 2-hour Post meal, Midday Premeal, Midday 2-hour Post meal, Evening Premeal, Evening 2-hour Post meal and Bedtime. The daily average was calculated as the average of the 7 blood glucose values collected on a particular day. LS mean was determined by MMRM model with variables Baseline + Pooled Country + Baseline Metformin Use (Yes, No) + Baseline HbA1c Group (<=8.5%, >8.5%) + Treatment + Time + Treatment*Time (Type III sum of squares). APD: All randomly assigned participants who took at least 1 dose of study drug and had a baseline and at least 1 post-baseline value for this analysis, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or prematurely stopping study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Lispro
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	219	210	204	574
Units: mg/dL/day				
least squares mean (standard error)	-56.7 (± 1.80)	-61.5 (± 1.85)	67.6 (± 1.86)	-55.8 (± 1.13)

Statistical analyses

Statistical analysis title	Outcome measure 6
Comparison groups	5 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	793
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.682
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	3.3

Statistical analysis title	Outcome measure 6
Comparison groups	10 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	784
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-5.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.9
upper limit	-1.4

Statistical analysis title	Outcome measure 6
Comparison groups	15 mg Tirzepatide v Insulin Lispro

Number of subjects included in analysis	778
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-11.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16
upper limit	-7.5

Secondary: Percentage of Participants who Achieved HbA1c Target Value of <7.0% without Hypoglycemia

End point title	Percentage of Participants who Achieved HbA1c Target Value of <7.0% without Hypoglycemia

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. APD: All randomly assigned participants who took at least 1 dose of study drug and had a baseline and at least 1 post-baseline value for this analysis, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or prematurely stopping study drug.

End point type	Secondary

End point timeframe:

Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Lispro
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	241	234	233	692
Units: Percentage of HbA1c				
number (not applicable)	52.70	70.05	75.12	13.41

Statistical analyses

Statistical analysis title	Outcome measure 7
Comparison groups	5 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	933
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	8.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	5.66
upper limit	11.83

Statistical analysis title	Outcome measure 7
Comparison groups	10 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	926
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	16.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.44
upper limit	24.96

Statistical analysis title	Outcome measure 7
Comparison groups	15 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	925
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	21.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.49
upper limit	32.93

Secondary: Percentage of Participants who Achieved Weight Loss ≥5%

End point title	Percentage of Participants who Achieved Weight Loss ≥5%

End point description:

Percentage of Participants who Achieved Weight Loss ≥5% is reported here. APD: All randomly assigned participants who took at least 1 dose of study drug and had a baseline and at least 1 post-baseline value for this analysis, excluding participants discontinuing study drug due to inadvertent enrollment and data after initiating rescue antihyperglycemic medication or prematurely stopping study drug.

End point type	Secondary

End point timeframe:
Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Lispro
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	242	238	236	708
Units: Percentage of participants				
number (not applicable)	64.19	79.21	83.15	6.34

Statistical analyses

Statistical analysis title	Outcome measure 8
Comparison groups	5 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	950
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	28.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.36
upper limit	43.46

Statistical analysis title	Outcome measure 8
Comparison groups	10 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	946
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	58.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	36.76
upper limit	94.39

Statistical analysis title	Outcome measure 8
Comparison groups	15 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	944
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	77.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	47.49
upper limit	127.33

Secondary: Change from Baseline in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) Score

End point title	Change from Baseline in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) Score

End point description:

The SF-36 is a health-related survey that assesses participant's quality of life and consists of 36 questions covering 8 health domains: physical functioning, bodily pain, role limitations due to physical problems and emotional problems, general health, mental health, social functioning, vitality, and two overall summary scores: physical component summary (PCS) and mental component summary (MCS) scores. PCS consisted of physical functioning, bodily pain, role-physical, and general health scales. PCS score is reported here. PCS domain is scored by summing individual items and transforming scores into a 0 to 100 scale with higher scores indicating better health status or functioning. LS mean was determined by analysis of covariance (ANCOVA) model with variables Baseline + Pooled Country + Baseline Metformin Use (Yes, No) + Baseline HbA1c Group (<=8.5%, >8.5%) + Treatment (Type III sum of squares). APD: All randomly assigned participants who took at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Lispro
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	222	217	199	599
Units: score on a scale				
least squares mean (standard error)	1.0 (± 0.46)	1.7 (± 0.46)	1.7 (± 0.48)	-0.6 (± 0.28)

Statistical analyses

Statistical analysis title	Outcome measure 9
Comparison groups	5 mg Tirzepatide v Insulin Lispro

Number of subjects included in analysis	821
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	2.6

Statistical analysis title	Outcome measure 9
Comparison groups	10 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	816
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	3.3

Statistical analysis title	Outcome measure 9
Comparison groups	15 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	798
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	3.3

Secondary: Change from Baseline in 36-Item SF-36 Mental Component Summary

(MCS) Score	
End point title	Change from Baseline in 36-Item SF-36 Mental Component Summary (MCS) Score

End point description:

The SF-36 is a health-related survey that assesses participant's quality of life and consists of 36 questions covering 8 health domains: physical functioning, bodily pain, role limitations due to physical problems and emotional problems, general health, mental health, social functioning, vitality, and two overall summary scores: physical component summary (PCS) and mental component summary (MCS) scores. MCS consisted of social functioning, vitality, mental health, and role-emotional scales. MCS score is reported here. MCS domain is scored by summing individual items and transforming scores into a 0 to 100 scale with higher scores indicating better health status or functioning. LS mean was determined by ANCOVA model with variables Baseline + Pooled Country + Baseline Metformin Use (Yes, No) + Baseline HbA1c Group (<=8.5%, >8.5%) + Treatment (Type III sum of squares). APD: All randomly assigned participants who took at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Lispro
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	222	217	199	599
Units: score on a scale				
least squares mean (standard error)	0.3 (± 0.59)	1.5 (± 0.59)	0.7 (± 0.62)	-1.3 (± 0.36)

Statistical analyses

Statistical analysis title	Outcome measure 10
Comparison groups	5 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	821
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	2.9

Statistical analysis title	Outcome measure 10
Comparison groups	10 mg Tirzepatide v Insulin Lispro

Number of subjects included in analysis	816
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	4.2

Statistical analysis title	Outcome measure 10
Comparison groups	15 mg Tirzepatide v Insulin Lispro
Number of subjects included in analysis	798
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	3.5

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to week 56	
Adverse event reporting additional description:	
All randomized participants who received at least one dose of study drug. Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	5 mg Tirzepatide
Reporting group description:	
Participants received 5 mg tirzepatide administered SC once a week	
Reporting group title	Insulin Lispro
Reporting group description:	
Participants received Insulin lispro (U100) administered SC three times a day.	
Reporting group title	15 mg Tirzepatide
Reporting group description:	
Participants received 15 mg tirzepatide administered SC once a week.	
Reporting group title	10 mg Tirzepatide
Reporting group description:	
Participants received 10 mg tirzepatide administered SC once a week.	

Serious adverse events	5 mg Tirzepatide	Insulin Lispro	15 mg Tirzepatide
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 243 (8.23%)	81 / 708 (11.44%)	17 / 236 (7.20%)
number of deaths (all causes)	3	11	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenocarcinoma of colon			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (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
breast cancer			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
glioblastoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
lipoma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	0 / 236 (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
oral neoplasm			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
lung neoplasm malignant			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	2 / 708 (0.28%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
small cell lung cancer			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (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
Vascular disorders			
giant cell arteritis			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral arterial occlusive disease			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	1 / 708 (0.14%)	0 / 236 (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
peripheral ischaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	0 / 236 (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
peripheral vascular disorder			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
Surgical and medical procedures			
aortic valve replacement			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (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
arthrodesis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
coronary artery bypass			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
retinal cryoablation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
umbilical hernia repair			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
Pregnancy, puerperium and perinatal conditions			
abortion spontaneous			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed[1]	1 / 144 (0.69%)	0 / 396 (0.00%)	0 / 133 (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
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
death			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	1 / 708 (0.14%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
hypothermia			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (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
Respiratory, thoracic and mediastinal disorders			
pulmonary embolism			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (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
pulmonary mass			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	2 / 708 (0.28%)	0 / 236 (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
pulmonary oedema			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory failure			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
Psychiatric disorders			
bipolar disorder			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (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
mental status changes			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
suicide attempt			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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			
spinal fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (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
spinal compression fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
skull fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
angina unstable			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 243 (0.00%)	3 / 708 (0.42%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
arteriosclerosis coronary artery			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (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
acute myocardial infarction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	2 / 708 (0.28%)	0 / 236 (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
atrial fibrillation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac failure			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac failure congestive			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
coronary artery disease			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	3 / 708 (0.42%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

myocardial ischaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myocardial infarction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	3 / 708 (0.42%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Nervous system disorders			
cerebrovascular accident			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	1 / 708 (0.14%)	0 / 236 (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
cerebellar infarction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	0 / 236 (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 25.1			
subjects affected / exposed	0 / 243 (0.00%)	2 / 708 (0.28%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoglycaemic coma			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	2 / 708 (0.28%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ischaemic stroke			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	2 / 236 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transient ischaemic attack			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (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			
iron deficiency anaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
colonic fistula			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
colitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
diverticulum intestinal haemorrhagic			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diabetic gastropathy			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	0 / 236 (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
gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
lower gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	0 / 236 (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
Hepatobiliary disorders			
cholelithiasis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	0 / 236 (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
cholecystitis acute			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
cholecystitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
diabetic foot			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 243 (0.41%)	1 / 708 (0.14%)	0 / 236 (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
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal mass			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
inappropriate antidiuretic hormone secretion			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
intervertebral disc protrusion			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	0 / 236 (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
osteoarthritis			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spinal disorder			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
bullous erysipelas			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
covid-19			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	7 / 708 (0.99%)	2 / 236 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
covid-19 pneumonia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 243 (0.82%)	7 / 708 (0.99%)	2 / 236 (0.85%)
occurrences causally related to treatment / all	0 / 2	0 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
gangrene			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (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
erysipelas			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 243 (0.82%)	0 / 708 (0.00%)	0 / 236 (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
gastroenteritis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diabetic foot infection			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	2 / 708 (0.28%)	0 / 236 (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
cystitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
diabetic gangrene			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (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
infected skin ulcer			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	0 / 236 (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 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (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
oophoritis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed[2]	0 / 144 (0.00%)	1 / 396 (0.25%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
postoperative abscess			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	1 / 708 (0.14%)	0 / 236 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	2 / 236 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
septic shock			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	0 / 236 (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
urinary tract infection			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 243 (0.41%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
hyperkalaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 243 (0.00%)	0 / 708 (0.00%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoglycaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 243 (0.82%)	28 / 708 (3.95%)	1 / 236 (0.42%)
occurrences causally related to treatment / all	1 / 2	25 / 84	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	10 mg Tirzepatide		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 238 (6.72%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenocarcinoma of colon			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
breast cancer			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
glioblastoma			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lipoma				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	1 / 238 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
oral neoplasm				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lung neoplasm malignant				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
small cell lung cancer				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
giant cell arteritis				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
peripheral arterial occlusive disease				
alternative dictionary used: MedDRA 25.1				

subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
peripheral ischaemia				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	1 / 238 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
peripheral vascular disorder				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
aortic valve replacement				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
arthrodesis				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
coronary artery bypass				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
retinal cryoablation				
alternative dictionary used: MedDRA 25.1				

subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
umbilical hernia repair				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pregnancy, puerperium and perinatal conditions				
abortion spontaneous				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed[1]	0 / 149 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
asthenia				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
death				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypothermia				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
pulmonary embolism				
alternative dictionary used:				

MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pulmonary mass				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pulmonary oedema				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
respiratory failure				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
bipolar disorder				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
mental status changes				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
suicide attempt				
alternative dictionary used: MedDRA 25.1				

subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
spinal fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
spinal compression fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
skull fracture			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
angina unstable			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
arteriosclerosis coronary artery			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
acute myocardial infarction			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 238 (0.84%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
atrial fibrillation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 238 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
cardiac failure			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
cardiac failure congestive			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (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 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
myocardial ischaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

myocardial infarction				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
cerebrovascular accident				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cerebellar infarction				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	1 / 238 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
hypoglycaemic unconsciousness				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypoglycaemic coma				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ischaemic stroke				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	1 / 238 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
transient ischaemic attack				
alternative dictionary used: MedDRA 25.1				

subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
iron deficiency anaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
colonic fistula			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
colitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (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 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
diabetic gastropathy			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 238 (0.42%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 238 (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 25.1			
subjects affected / exposed	1 / 238 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
cholelithiasis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 238 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
cholecystitis acute			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 238 (0.42%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
cholecystitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
diabetic foot			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	1 / 238 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
renal mass				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (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 25.1				
subjects affected / exposed	0 / 238 (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 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
intervertebral disc protrusion				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	1 / 238 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
osteoarthritis				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
spinal disorder				
alternative dictionary used: MedDRA 25.1				

subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
bullous erysipelas			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
covid-19			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	1 / 238 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
covid-19 pneumonia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	2 / 238 (0.84%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
gangrene			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
erysipelas			
alternative dictionary used: MedDRA 25.1			

subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastroenteritis				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
diabetic foot infection				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cystitis				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
diabetic gangrene				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
infected skin ulcer				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	1 / 238 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
osteomyelitis				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

oophoritis				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed[2]	0 / 149 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
postoperative abscess				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pneumonia				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	1 / 238 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
sepsis				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
septic shock				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
urinary tract infection				
alternative dictionary used: MedDRA 25.1				
subjects affected / exposed	0 / 238 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
hyperkalaemia				
alternative dictionary used: MedDRA 25.1				

subjects affected / exposed	0 / 238 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
hypoglycaemia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	3 / 238 (1.26%)		
occurrences causally related to treatment / all	1 / 18		
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: Gender specific events only occurring in male or female participants have had the number of participants at risk 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: Gender specific events only occurring in male or female participants have had the number of participants at risk adjusted accordingly.

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

Non-serious adverse events	5 mg Tirzepatide	Insulin Lispro	15 mg Tirzepatide
Total subjects affected by non-serious adverse events			
subjects affected / exposed	94 / 243 (38.68%)	99 / 708 (13.98%)	121 / 236 (51.27%)
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	6 / 243 (2.47%)	4 / 708 (0.56%)	14 / 236 (5.93%)
occurrences (all)	9	9	19
vomiting			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	11 / 243 (4.53%)	4 / 708 (0.56%)	30 / 236 (12.71%)
occurrences (all)	14	4	80
dyspepsia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	15 / 243 (6.17%)	4 / 708 (0.56%)	27 / 236 (11.44%)
occurrences (all)	16	4	34
nausea			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	33 / 243 (13.58%)	8 / 708 (1.13%)	61 / 236 (25.85%)
occurrences (all)	71	11	161

diarrhoea			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	29 / 243 (11.93%)	17 / 708 (2.40%)	26 / 236 (11.02%)
occurrences (all)	46	22	49
Infections and infestations			
covid-19			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	28 / 243 (11.52%)	72 / 708 (10.17%)	21 / 236 (8.90%)
occurrences (all)	28	73	23
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	20 / 243 (8.23%)	1 / 708 (0.14%)	40 / 236 (16.95%)
occurrences (all)	81	1	128

Non-serious adverse events	10 mg Tirzepatide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	116 / 238 (48.74%)		
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	8 / 238 (3.36%)		
occurrences (all)	8		
vomiting			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	21 / 238 (8.82%)		
occurrences (all)	35		
dyspepsia			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	27 / 238 (11.34%)		
occurrences (all)	47		
nausea			
alternative dictionary used: MedDRA 25.1			
subjects affected / exposed	49 / 238 (20.59%)		
occurrences (all)	80		
diarrhoea			

alternative dictionary used: MedDRA 25.1 subjects affected / exposed occurrences (all)	 36 / 238 (15.13%) 66		
Infections and infestations covid-19 alternative dictionary used: MedDRA 25.1 subjects affected / exposed occurrences (all)	 19 / 238 (7.98%) 19		
Metabolism and nutrition disorders decreased appetite alternative dictionary used: MedDRA 25.1 subjects affected / exposed occurrences (all)	 28 / 238 (11.76%) 84		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2021	Protocol Amendment (b): Section 10.9. Appendix 9: An appendix was added describing the temporary measures intended to be used only in the case of exceptional circumstances during specific time periods as directed by the sponsor in partnership with the investigator. Section 5.2. Exclusion Criteria: Section 10.1.5 10.1.10; 1.2 Schema, Section 6.5: Minor errors in units, section numbering, abbreviations, and incorrect references were corrected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported