Clinical trial results:
Efficacy and Safety of LY3298176 Once Weekly versus Insulin Glargine in Patients with Type 2 Diabetes and Increased Cardiovascular Risk

Summary

EudraCT number	2018-002618-11
Trial protocol	GR ES PL RO
Global end of trial date	22 April 2021

Results information

Result version number	v1 (current)
This version publication date	06 February 2022
First version publication date	06 February 2022

Trial information

Trial identification

Sponsor protocol code	I8F-MC-GPGM

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03730662
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17072

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	22 April 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the trial is to assess the efficacy and safety of tirzepatide taken once a week to insulin glargine taken once daily in participants with type 2 diabetes and increased cardiovascular risk. The study will last about 108 weeks and may include up to 30 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	20 November 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 484
Country: Number of subjects enrolled	Australia: 19
Country: Number of subjects enrolled	Brazil: 250
Country: Number of subjects enrolled	Canada: 51
Country: Number of subjects enrolled	Greece: 38
Country: Number of subjects enrolled	Israel: 29
Country: Number of subjects enrolled	Mexico: 160
Country: Number of subjects enrolled	Poland: 156
Country: Number of subjects enrolled	Romania: 82
Country: Number of subjects enrolled	Russian Federation: 88
Country: Number of subjects enrolled	Slovakia: 199
Country: Number of subjects enrolled	Spain: 77
Country: Number of subjects enrolled	Taiwan: 30
Country: Number of subjects enrolled	United States: 339
Worldwide total number of subjects	2002
EEA total number of subjects	552

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)	1051
From 65 to 84 years	941
85 years and over	10

Subject disposition

Recruitment

Recruitment details:

No Text Available

Pre-assignment

Screening details:

No Text Available

Period 1

Period 1 title	Treatment Period (52 Weeks)
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:

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

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

Arm description:

15 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	Insulin Glargine

Arm description:

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

The starting dose of insulin glargine was 10 IU/day at bedtime, titrated to a FBG <100 mg/dL, following a treat-to-target (TTT) algorithm.

Arm type	Active comparator
Investigational medicinal product name	Insulin Glargine
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	329	330	338
Received at least one dose of study drug	329	328	338
Completed	308	319	329
Not completed	21	11	9
Adverse event, serious fatal	6	2	2
Physician decision	1	1	-
Consent withdrawn by subject	5	-	5
Screen Failure	-	1	-
Adverse event, non-fatal	3	2	-
Lost to follow-up	4	2	2
Personal Reason	2	2	-
Protocol deviation	-	1	-

Number of subjects in period 1	Insulin Glargine
Started	1005
Received at least one dose of study drug	1000
Completed	953
Not completed	52
Adverse event, serious fatal	9
Physician decision	3
Consent withdrawn by subject	23
Screen Failure	-
Adverse event, non-fatal	3
Lost to follow-up	11
Personal Reason	2

Protocol deviation	1

Period 2

Period 2 title	Variable Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	5 mg Tirzepatide

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

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

Arm description:

15 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	Insulin Glargine

Arm description:

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

The starting dose of insulin glargine was 10 IU/day at bedtime, titrated to a FBG <100 mg/dL, following a treat-to-target (TTT) algorithm.

Arm type	Active comparator
Investigational medicinal product name	Insulin Glargine
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 2	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide
Started	308	319	329
Completed	294	312	313
Not completed	14	7	16
Adverse event, serious fatal	9	-	6
Consent withdrawn by subject	2	1	4
Physician decision	-	-	-
Adverse event, non-fatal	1	2	-
Lost to follow-up	2	1	4
Personal Reason	-	2	1
Protocol deviation	-	1	1

Number of subjects in period 2	Insulin Glargine
Started	953
Completed	882
Not completed	71
Adverse event, serious fatal	26
Consent withdrawn by subject	17
Physician decision	3
Adverse event, non-fatal	7
Lost to follow-up	11
Personal Reason	6

Protocol deviation	1

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.	
Reporting group title	Insulin Glargine
Reporting group description:	
Insulin glargine administered SC once a day. Doses were individualized and titrated according to protocol-defined targets. The starting dose of insulin glargine was 10 IU/day at bedtime, titrated to a FBG <100 mg/dL, following a treat-to-target (TTT) algorithm.	

Reporting group values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide
Number of subjects	329	330	338
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	62.90	63.70	63.70
standard deviation	± 8.56	± 8.68	± 8.60
Gender categorical Units: Subjects			
Female	131	121	135
Male	198	209	203
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	154	164	155
Not Hispanic or Latino	172	164	179
Unknown or Not Reported	3	2	4
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	32	30	26
Asian	15	16	8
Native Hawaiian or Other Pacific Islander	0	0	2
Black or African American	13	18	11
White	260	260	285
More than one race	8	6	5
Unknown or Not Reported	1	0	1
Region of Enrollment Units: Subjects			

Argentina	80	80	82
Australia	3	3	4
Brazil	42	41	42
Canada	8	9	7
Greece	7	5	7
Israel	4	5	5
Mexico	27	27	26
Poland	27	25	26
Romania	13	14	14
Russia	14	14	15
Slovakia	33	32	34
Spain	11	14	14
Taiwan	5	5	5
United States	55	56	57
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	8.52	8.59	8.52
standard deviation	± 0.84	± 0.91	± 0.98

Reporting group values	Insulin Glargine	Total	
Number of subjects	1005	2002	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	63.80		
standard deviation	± 8.51	-	
Gender categorical			
Units: Subjects			
Female	364	751	
Male	641	1251	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	478	951	
Not Hispanic or Latino	521	1036	
Unknown or Not Reported	6	15	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	86	174	
Asian	31	70	
Native Hawaiian or Other Pacific Islander	1	3	
Black or African American	34	76	
White	827	1632	
More than one race	24	43	
Unknown or Not Reported	2	4	
Region of Enrollment			
Units: Subjects			
Argentina	242	484	

Australia	9	19	
Brazil	125	250	
Canada	27	51	
Greece	19	38	
Israel	15	29	
Mexico	80	160	
Poland	78	156	
Romania	41	82	
Russia	45	88	
Slovakia	100	199	
Spain	38	77	
Taiwan	15	30	
United States	171	339	
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	8.50		
standard deviation	± 0.85	-	

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.	
Reporting group title	Insulin Glargine
Reporting group description:	
Insulin glargine administered SC once a day. Doses were individualized and titrated according to protocol-defined targets. The starting dose of insulin glargine was 10 IU/day at bedtime, titrated to a FBG <100 mg/dL, following a treat-to-target (TTT) algorithm.	
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.	
Reporting group title	Insulin Glargine
Reporting group description:	
Insulin glargine administered SC once a day. Doses were individualized and titrated according to protocol-defined targets. The starting dose of insulin glargine was 10 IU/day at bedtime, titrated to a FBG <100 mg/dL, following a treat-to-target (TTT) algorithm.	

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 for post-baseline measures: Variable = Baseline + Pooled Country + Baseline sodium-glucose co-transporter-2 inhibitor (SGLT-2i) use Flag (Yes, No) + 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.	
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 Glargine	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	289	291	887	
Units: Percentage of HbA1c				
least squares mean (standard error)	-2.43 (± 0.053)	-2.58 (± 0.053)	-1.44 (± 0.030)	

Statistical analyses

Statistical analysis title	HbA1c (10 mg Tirzepatide, Insulin Glargine)
Comparison groups	10 mg Tirzepatide v Insulin Glargine
Number of subjects included in analysis	1176
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.99
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.13
upper limit	-0.86

Notes:

[2] - Although the primary objective is to establish noninferiority, sample size selection is guided by the objective of establishing superiority. The chosen sample size and randomization ratio also provides >90% power to establish superiority of 10 mg LY3298176 and 15 mg LY3298176 doses to insulin glargine in absence of confounding effects of rescue therapy for persistent severe hyperglycemia ("efficacy" estimand).

Statistical analysis title	HbA1c (15 mg Tirzepatide, Insulin Glargine)
Comparison groups	15 mg Tirzepatide v Insulin Glargine
Number of subjects included in analysis	1178
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-1.14
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.28
upper limit	-1

Notes:

[3] - Although the primary objective is to establish noninferiority, sample size selection is guided by the objective of establishing superiority. The chosen sample size and randomization ratio also provides >90% power to establish superiority of 10 mg LY3298176 and 15 mg LY3298176 doses to insulin glargine in absence of confounding effects of rescue therapy for persistent severe hyperglycemia ("efficacy" estimand).

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. LS mean was determined by MMRM model for post-baseline measures: Variable = Baseline + Pooled Country + Baseline SGLT-2i use Flag (Yes, No) + 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.

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 Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	887		
Units: Percentage of HbA1c				
least squares mean (standard error)	-2.24 (± 0.053)	-1.44 (± 0.030)		

Statistical analyses

Statistical analysis title	HbA1c (5 mg Tirzepatide, Insulin Glargine)
Comparison groups	5 mg Tirzepatide v Insulin Glargine
Number of subjects included in analysis	1170
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.8
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.93
upper limit	-0.66

Notes:

[5] - Although the primary objective is to establish noninferiority, sample size selection is guided by the objective of establishing superiority. The chosen sample size and randomization ratio also provides >90% power to establish superiority of 10 mg LY3298176 and 15 mg LY3298176 doses to insulin glargine in absence of confounding effects of rescue therapy for persistent severe hyperglycemia

("efficacy" estimand).

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 for post-baseline measures: Variable = Baseline + Pooled Country + Baseline HbA1c Group (<=8.5%, >8.5%) + Baseline SGLT-2i use Flag (Yes, No) + 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.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Glargine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	285	288	291	891
Units: Kilograms (kg)				
least squares mean (standard error)	-7.1 (± 0.34)	-9.5 (± 0.34)	-11.7 (± 0.33)	1.9 (± 0.19)

Statistical analyses

Statistical analysis title	Body Weight (5 mg Tirzepatide, Insulin Glargine)
Comparison groups	5 mg Tirzepatide v Insulin Glargine
Number of subjects included in analysis	1176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.8
upper limit	-8.3

Statistical analysis title	Body Weight (10 mg Tirzepatide, Insulin Glargine)
Comparison groups	10 mg Tirzepatide v Insulin Glargine

Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-11.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.1
upper limit	-10.6

Statistical analysis title	Body Weight (15 mg Tirzepatide, Insulin Glargine)
Comparison groups	15 mg Tirzepatide v Insulin Glargine
Number of subjects included in analysis	1182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-13.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.3
upper limit	-12.8

Secondary: Percentage of Participants with HbA1c of <7.0%

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

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. Imputed data includes observed value and imputed value if endpoint measure is missing.

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

End point type	Secondary

End point timeframe:

Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Glargine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	326	321	334	978
Units: percentage of participants				
number (not applicable)	80.98	88.16	90.72	50.72

Statistical analyses

Statistical analysis title	HbA1c of <7.0% (5 mg Tirzepatide,Insulin Glargin)
Comparison groups	5 mg Tirzepatide v Insulin Glargine
Number of subjects included in analysis	1304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.47
upper limit	6.58

Statistical analysis title	HbA1c of <7.0% (10 mg Tirzepatide,Insulin Glargin)
Comparison groups	10 mg Tirzepatide v Insulin Glargine
Number of subjects included in analysis	1299
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	9.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.31
upper limit	13.49

Statistical analysis title	HbA1c of <7.0% (15 mg Tirzepatide,Insulin Glargin)
Comparison groups	15 mg Tirzepatide v Insulin Glargine

Number of subjects included in analysis	1312
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.88
upper limit	17.89

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 for post-baseline measures: Variable = Baseline + Pooled Country + Baseline HbA1c Group (<=8.5%, >8.5%) + Baseline SGLT-2i use Flag (Yes, No) + 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.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Glargine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	281	283	288	880
Units: milligram per Deciliter (mg/dL)				
least squares mean (standard error)	-50.4 (± 2.07)	-54.9 (± 2.06)	-59.3 (± 2.04)	-51.4 (± 1.17)

Statistical analyses

Statistical analysis title	Fasting Glucose(5 mg Tirzepatide,Insulin Glargine)
Comparison groups	5 mg Tirzepatide v Insulin Glargine
Number of subjects included in analysis	1161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.672
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	5.7

Statistical analysis title	Fasting Glucose(10mg Tirzepatide,Insulin Glargine)
Comparison groups	Insulin Glargine v 10 mg Tirzepatide
Number of subjects included in analysis	1163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.134
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.2
upper limit	1.1

Statistical analysis title	Fasting Glucose(15mg Tirzepatide,Insulin Glargine)
Comparison groups	Insulin Glargine v 15 mg Tirzepatide
Number of subjects included in analysis	1168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.6
upper limit	-3.4

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

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 + Pooled Country + Baseline HbA1c Group (<=8.5%,

>8.5%) + Baseline SGLT-2i use Flag (Yes, No) + Treatment + Time + Treatment*Time (Type III sum of squares).

Analysis Population Description: All randomized participants who received at least one dose of study drug, excluding participants discontinuing study drug due to inadvertent enrollment.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Glargine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	265	261	265	784
Units: mg/dL				
least squares mean (standard error)	-58.4 (± 1.65)	-61.1 (± 1.66)	-66.1 (± 1.66)	-46.1 (± 0.96)

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Steady State Area Under the Concentration Time Curve From Zero to Tau (AUC 0-Tau) of Tirzepatide

End point title	Pharmacokinetics (PK): Steady State Area Under the Concentration Time Curve From Zero to Tau (AUC 0-Tau) of Tirzepatide[6]

End point description:

Pharmacokinetics (PK): Steady State Area Under the Concentration Time Curve From Zero to Tau (AUC 0-Tau) of Tirzepatide

Analysis Population Description:Pharmacokinetic samples were collected from atleast the first 150 participants at each Tirzepatide dose, all participants aged ≥70 years, and all participants with severe renal impairment or end-stage renal disease (ESRD) (estimated glomerular filtration rate [eGFR] <30 mL/min).

End point type	Secondary

End point timeframe:

1 to 24 hours, 24 to 96 hours, or 120 to 168 hours post dose of Week 7, 15, 23, 35

Notes:

[6] - 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 Tirzepatide arms only.

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	326	324	334	
Units: Nanograms per millilitre per hour				
geometric mean (geometric coefficient of variation)	81800 (± 23.9)	165000 (± 20.3)	246000 (± 20.6)	

Statistical analyses

No statistical analyses for this end point

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

End point description:

The 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. Post-baseline comparisons between treatment and control group was evaluated using negative binomial model with variables : Number of episodes = Baseline HbA1c Group (<=8.5%, >8.5%) + Pooled Country + Baseline SGLT-2i use Flag (Yes, No) + Treatment, with log (exposure in days/365.25) as an offset variable.

Analysis Population Description: All randomized participants who received at least one dose of study drug, excluding participants hypoglycemic events occurring after initiation of a new antihyperglycemic therapy

End point type	Secondary

End point timeframe:

Baseline through Week 52

End point values	5 mg Tirzepatide	10 mg Tirzepatide	15 mg Tirzepatide	Insulin Glargine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	329	328	338	1000
Units: Episodes/participant/365.25 days				
arithmetic mean (standard error)	0.10 (± 0.023)	0.09 (± 0.025)	0.11 (± 0.030)	0.35 (± 0.044)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline Up To 2 Years	
Adverse event reporting additional description:	
All participants who received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	5 mg Tirzepatide
Reporting group description:	
5 milligrams (mg) tirzepatide administered subcutaneously (SC) once a week.	
Reporting group title	15 mg Tirzepatide
Reporting group description:	
15 mg tirzepatide administered SC once a week.	
Reporting group title	Insulin Glargine
Reporting group description:	
Insulin glargine administered SC once a day. Doses were individualized and titrated according to protocol-defined targets. The starting dose of insulin glargine was 10 IU/day at bedtime, titrated to a FBG <100 mg/dL, following a treat-to-target (TTT) algorithm.	
Reporting group title	10 mg Tirzepatide
Reporting group description:	
10 mg tirzepatide administered SC once a week.	

Serious adverse events	5 mg Tirzepatide	15 mg Tirzepatide	Insulin Glargine
Total subjects affected by serious adverse events			
subjects affected / exposed	48 / 329 (14.59%)	41 / 338 (12.13%)	193 / 1000 (19.30%)
number of deaths (all causes)	15	8	35
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 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bile duct adenocarcinoma			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bladder transitional cell carcinoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
breast cancer stage ii			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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 cancer metastatic			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
glioblastoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
invasive lobular breast carcinoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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

laryngeal squamous cell carcinoma alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lung adenocarcinoma alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
lung neoplasm malignant alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
meningioma alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
metastases to liver alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
metastases to lymph nodes alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
metastatic squamous cell carcinoma alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
nasopharyngeal cancer			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
neoplasm malignant			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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
non-hodgkin's lymphoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ovarian cancer			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed[1]	0 / 131 (0.00%)	1 / 135 (0.74%)	0 / 364 (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
pancreatic carcinoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
pancreatic neoplasm			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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

papillary renal cell carcinoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
prostate cancer			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed[2]	0 / 198 (0.00%)	1 / 203 (0.49%)	3 / 636 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal cancer recurrent			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
renal cell carcinoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
squamous cell carcinoma of lung			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
aortic aneurysm			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
aortic aneurysm rupture			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
arteriosclerosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
deep vein thrombosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypertension			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypotension			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
iliac artery stenosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral arterial occlusive disease			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

peripheral artery occlusion			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
peripheral ischaemia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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 vascular disorder			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombophlebitis superficial			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
coronary artery bypass			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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
intervertebral disc operation			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
spinal fusion surgery			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	2 / 338 (0.59%)	0 / 1000 (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
chest pain			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
death			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	1 / 338 (0.30%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 2
necrosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
non-cardiac chest pain			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
pyrexia			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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
sudden cardiac death			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
sudden death			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
systemic inflammatory response syndrome			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
Reproductive system and breast disorders			
ovarian cyst			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed[3]	0 / 131 (0.00%)	0 / 135 (0.00%)	1 / 364 (0.27%)
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			
acute pulmonary oedema			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
acute respiratory distress syndrome			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
acute respiratory failure			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	3 / 1000 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
asthma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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
asthmatic crisis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	3 / 1000 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dyspnoea			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
epistaxis			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoxia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
interstitial lung disease			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumothorax			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary embolism			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	3 / 1000 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
pulmonary fibrosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary mass			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
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 failure			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	4 / 1000 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 4
Psychiatric disorders			
confusional state			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
disorientation			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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			
blood creatinine increased			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
blood lactic acid increased			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
influenza a virus test positive			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatic enzymes increased			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
concussion			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
fall			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
femoral neck fracture			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hand fracture			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
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 / 329 (0.00%)	1 / 338 (0.30%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
humerus fracture			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
joint dislocation			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ligament injury			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
limb injury			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
meniscus injury			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

nerve injury			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rib fracture			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spinal column injury			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
spinal compression fracture			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
subdural haematoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
thoracic vertebral fracture			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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
Congenital, familial and genetic disorders			
phimosis			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed[4]	1 / 198 (0.51%)	0 / 203 (0.00%)	0 / 636 (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 disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
acute left ventricular failure			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
acute myocardial infarction			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	3 / 329 (0.91%)	3 / 338 (0.89%)	18 / 1000 (1.80%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 19
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 2
angina pectoris			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	3 / 1000 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
angina unstable			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	1 / 338 (0.30%)	6 / 1000 (0.60%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
aortic valve sclerosis			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
arteriosclerosis coronary artery			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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 fibrillation			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	1 / 338 (0.30%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrial flutter			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrial tachycardia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
atrioventricular block			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrioventricular block second degree			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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 / 329 (0.30%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
cardiac disorder			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
cardiac failure			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	2 / 329 (0.61%)	2 / 338 (0.59%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
cardiac failure acute			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac failure chronic			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
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 congestive			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	5 / 1000 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
cardio-respiratory arrest			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	1 / 329 (0.30%)	1 / 338 (0.30%)	0 / 1000 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
cardiogenic shock			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
cardiomyopathy			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
coronary artery disease			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	5 / 329 (1.52%)	2 / 338 (0.59%)	15 / 1000 (1.50%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 16
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
coronary artery stenosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ischaemic cardiomyopathy			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
left ventricular failure			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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

myocardial infarction alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	3 / 329 (0.91%)	1 / 338 (0.30%)	4 / 1000 (0.40%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
myocardial ischaemia alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myocarditis alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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
supraventricular extrasystoles alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
supraventricular tachycardia alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ventricular dysfunction alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
ventricular extrasystoles alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
Nervous system disorders			
carpal tunnel syndrome			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cerebellar stroke			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
cerebrovascular accident			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	1 / 338 (0.30%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cognitive disorder			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
coma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cranial nerve disorder			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
dizziness			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
encephalopathy			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
guillain-barre syndrome			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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
haemorrhagic stroke			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	2 / 329 (0.61%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
headache			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
hemiplegia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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

hypoxic-ischaemic encephalopathy alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ischaemic stroke alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	2 / 329 (0.61%)	1 / 338 (0.30%)	6 / 1000 (0.60%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lacunar infarction alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lacunar stroke alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lumbar radiculopathy alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
metabolic encephalopathy alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myelopathy alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
neuropathy peripheral			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
presyncope			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spinal cord compression			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 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 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
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 / 329 (0.00%)	1 / 338 (0.30%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thalamic infarction			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

transient ischaemic attack			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	3 / 1000 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bicytopenia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypochromic anaemia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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			
retinal vein occlusion			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
vitreous haemorrhage			

alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal hernia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
abdominal pain upper			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
abdominal wall haematoma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
duodenal ulcer			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
dysphagia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastric polyps			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
gastric ulcer			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
gastritis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
inguinal hernia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
obstructive pancreatitis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
pancreatitis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	2 / 329 (0.61%)	0 / 338 (0.00%)	0 / 1000 (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
pancreatitis acute			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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

peptic ulcer			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
biliary dilatation			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholangitis acute			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholecystitis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholecystitis acute			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hepatic cirrhosis			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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
hepatic function abnormal			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hepatitis acute			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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
hepatotoxicity			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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
Skin and subcutaneous tissue disorders			
diabetic foot			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	3 / 1000 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
skin necrosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
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 and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	2 / 329 (0.61%)	0 / 338 (0.00%)	3 / 1000 (0.30%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bladder mass			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
chronic kidney disease			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haematuria			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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
hydronephrosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
nephrolithiasis			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal cyst			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	1 / 338 (0.30%)	1 / 1000 (0.10%)
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 failure			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal impairment			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
renal infarct			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
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 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ureterolithiasis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

urinary bladder polyp			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
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			
arthropathy			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
intervertebral disc disorder			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intervertebral disc protrusion			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteoarthritis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pain in extremity			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
spinal osteoarthritis			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
systemic lupus erythematosus			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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
asymptomatic covid-19			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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
bronchitis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
covid-19			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	2 / 329 (0.61%)	2 / 338 (0.59%)	10 / 1000 (1.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 10
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 5
covid-19 pneumonia			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	2 / 329 (0.61%)	3 / 338 (0.89%)	15 / 1000 (1.50%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 15
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 3
cellulitis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
diabetic foot infection			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
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	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
erysipelas			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	3 / 1000 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fournier's gangrene			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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	0 / 329 (0.00%)	0 / 338 (0.00%)	2 / 1000 (0.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

hiv infection			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
infected skin ulcer			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
infection			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
liver abscess			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nosocomial infection			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
pneumonia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	2 / 338 (0.59%)	10 / 1000 (1.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia bacterial			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia klebsiella			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
postoperative wound infection			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
pyelonephritis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
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 tract infection			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	4 / 1000 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
septic shock			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	0 / 1000 (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

urinary tract infection			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	1 / 338 (0.30%)	3 / 1000 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urosepsis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	2 / 329 (0.61%)	2 / 338 (0.59%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
wound infection			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	0 / 1000 (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
Metabolism and nutrition disorders			
dehydration			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	2 / 329 (0.61%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diabetes mellitus inadequate control			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hyperkalaemia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoglycaemia			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	1 / 329 (0.30%)	3 / 338 (0.89%)	12 / 1000 (1.20%)
occurrences causally related to treatment / all	1 / 1	1 / 5	10 / 15
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypokalaemia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hyponatraemia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 338 (0.00%)	1 / 1000 (0.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
iron deficiency			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 338 (0.00%)	0 / 1000 (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

Serious adverse events	10 mg Tirzepatide		
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 328 (16.46%)		
number of deaths (all causes)	2		
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	1 / 328 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
bile duct adenocarcinoma			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
bladder transitional cell carcinoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
breast cancer stage ii				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
colon cancer metastatic				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
glioblastoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
invasive lobular breast carcinoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

laryngeal squamous cell carcinoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lung adenocarcinoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
meningioma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
metastases to lymph nodes				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
metastatic squamous cell carcinoma				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
nasopharyngeal cancer				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
neoplasm malignant				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
non-hodgkin's lymphoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ovarian cancer				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed[1]	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pancreatic carcinoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pancreatic neoplasm				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

papillary renal cell carcinoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
prostate cancer				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed[2]	0 / 209 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
renal cancer recurrent				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
renal cell carcinoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
squamous cell carcinoma of lung				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
aortic aneurysm				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
aortic aneurysm rupture				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
arteriosclerosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
deep vein thrombosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
hypertension			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 328 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
hypotension			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
iliac artery stenosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (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 23.1			
subjects affected / exposed	2 / 328 (0.61%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

peripheral artery occlusion				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
peripheral ischaemia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
peripheral vascular disorder				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
thrombophlebitis superficial				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
coronary artery bypass				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
intervertebral disc operation				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
spinal fusion surgery				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	0 / 328 (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 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
chest pain			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
death			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
necrosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 328 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
non-cardiac chest pain			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
pyrexia			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
sudden cardiac death				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
sudden death				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
systemic inflammatory response syndrome				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
ovarian cyst				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed[3]	0 / 119 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
acute pulmonary oedema				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
acute respiratory distress syndrome				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
acute respiratory failure			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
asthma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
asthmatic crisis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
dyspnoea			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
epistaxis			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypoxia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
interstitial lung disease				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pneumothorax				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pulmonary embolism				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pulmonary fibrosis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pulmonary mass				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

respiratory failure				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
confusional state				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
disorientation				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
blood creatinine increased				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
blood lactic acid increased				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
influenza a virus test positive				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pancreatic enzymes increased				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 328 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
concussion			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
fall			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
femoral neck fracture			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (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 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
hand fracture			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 328 (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 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
humerus fracture				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
joint dislocation				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ligament injury				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
limb injury				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
meniscus injury				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

nerve injury				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
rib fracture				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
spinal column injury				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
subdural haematoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
thoracic vertebral fracture				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
phimosis				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed[4]	0 / 209 (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 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
acute left ventricular failure			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (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 23.1			
subjects affected / exposed	7 / 328 (2.13%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
angina pectoris			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
angina unstable			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	2 / 328 (0.61%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
aortic valve sclerosis			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
arteriosclerosis coronary artery				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
atrial fibrillation				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	2 / 328 (0.61%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
atrial flutter				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
atrioventricular block				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
atrioventricular block second degree				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cardiac disorder				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cardiac failure acute				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cardiac failure chronic				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
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	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cardio-respiratory arrest				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
cardiogenic shock			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
cardiomyopathy			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (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	4 / 328 (1.22%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
coronary artery stenosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ischaemic cardiomyopathy			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
left ventricular failure			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

myocardial infarction				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
myocardial ischaemia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
myocarditis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
supraventricular extrasystoles				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
supraventricular tachycardia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ventricular dysfunction				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ventricular extrasystoles				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	1 / 328 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
carpal tunnel syndrome			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
cerebellar stroke			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 328 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
cerebrovascular accident			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
cognitive disorder			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
coma			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
cranial nerve disorder			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
dizziness				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
encephalopathy				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
guillain-barre syndrome				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
haemorrhagic stroke				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
headache				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hemiplegia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

hypoxic-ischaemic encephalopathy alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ischaemic stroke alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	4 / 328 (1.22%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
lacunar infarction alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lacunar stroke alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lumbar radiculopathy alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
metabolic encephalopathy alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
myelopathy alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
neuropathy peripheral				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
presyncope				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
spinal cord compression				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
subarachnoid haemorrhage				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
thalamic infarction				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

transient ischaemic attack			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	2 / 328 (0.61%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 328 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
bicytopenia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
hypochromic anaemia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	1 / 328 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
retinal vein occlusion			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
vitreous haemorrhage			

alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
abdominal hernia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
abdominal pain upper				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
abdominal wall haematoma				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
duodenal ulcer				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
dysphagia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastric polyps				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
gastric ulcer				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
gastritis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
inguinal hernia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
obstructive pancreatitis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pancreatitis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
pancreatitis acute				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

peptic ulcer				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
vomiting				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
biliary dilatation				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cholangitis acute				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cholecystitis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
cholecystitis acute				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
hepatic cirrhosis				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hepatic function abnormal				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hepatitis acute				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hepatotoxicity				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
skin necrosis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
skin ulcer				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	0 / 328 (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 23.1			
subjects affected / exposed	1 / 328 (0.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
bladder mass			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
chronic kidney disease			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
haematuria			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
hydronephrosis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	0 / 328 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
nephrolithiasis			
alternative dictionary used: MedDRA 23.1			

subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
renal cyst				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
renal failure				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
renal impairment				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
renal infarct				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
renal mass				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ureterolithiasis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

urinary bladder polyp				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
arthropathy				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
intervertebral disc disorder				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
osteoarthritis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pain in extremity				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
spinal osteoarthritis				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
systemic lupus erythematosus				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
asymptomatic covid-19				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
bronchitis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
covid-19				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	2 / 328 (0.61%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
covid-19 pneumonia				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	6 / 328 (1.83%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
cellulitis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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 23.1				
subjects affected / exposed	0 / 328 (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 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
erysipelas				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
fournier's gangrene				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
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	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

hiv infection				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (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 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
infection				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
liver abscess				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
nosocomial infection				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pneumonia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
pneumonia bacterial				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pneumonia klebsiella				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
postoperative wound infection				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
pyelonephritis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
respiratory tract infection				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
sepsis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
septic shock				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

urinary tract infection				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
urosepsis				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
wound infection				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	1 / 328 (0.30%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
dehydration				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
diabetes mellitus inadequate control				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hyperkalaemia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypoglycaemia				
alternative dictionary used: MedDRA 23.1				

subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypokalaemia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hyponatraemia				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
iron deficiency				
alternative dictionary used: MedDRA 23.1				
subjects affected / exposed	0 / 328 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
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	15 mg Tirzepatide	Insulin Glargine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	112 / 329 (34.04%)	184 / 338 (54.44%)	192 / 1000 (19.20%)
Investigations			

lipase increased			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	10 / 329 (3.04%)	21 / 338 (6.21%)	18 / 1000 (1.80%)
occurrences (all)	11	25	18
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	17 / 329 (5.17%)	14 / 338 (4.14%)	5 / 1000 (0.50%)
occurrences (all)	17	14	5
diarrhoea			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	41 / 329 (12.46%)	74 / 338 (21.89%)	44 / 1000 (4.40%)
occurrences (all)	68	118	50
dyspepsia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	18 / 329 (5.47%)	26 / 338 (7.69%)	13 / 1000 (1.30%)
occurrences (all)	23	36	13
nausea			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	39 / 329 (11.85%)	76 / 338 (22.49%)	23 / 1000 (2.30%)
occurrences (all)	104	157	29
vomiting			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	16 / 329 (4.86%)	29 / 338 (8.58%)	15 / 1000 (1.50%)
occurrences (all)	18	62	16
Infections and infestations			
covid-19			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	13 / 329 (3.95%)	17 / 338 (5.03%)	49 / 1000 (4.90%)
occurrences (all)	14	17	49
nasopharyngitis			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	10 / 329 (3.04%)	16 / 338 (4.73%)	65 / 1000 (6.50%)
occurrences (all)	11	19	70
Metabolism and nutrition disorders			

decreased appetite			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	29 / 329 (8.81%)	35 / 338 (10.36%)	5 / 1000 (0.50%)
occurrences (all)	36	43	5

Non-serious adverse events	10 mg Tirzepatide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	158 / 328 (48.17%)		
Investigations			
lipase increased			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	13 / 328 (3.96%)		
occurrences (all)	15		
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	14 / 328 (4.27%)		
occurrences (all)	15		
diarrhoea			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	65 / 328 (19.82%)		
occurrences (all)	128		
dyspepsia			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	27 / 328 (8.23%)		
occurrences (all)	36		
nausea			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	53 / 328 (16.16%)		
occurrences (all)	91		
vomiting			
alternative dictionary used: MedDRA 23.1			
subjects affected / exposed	27 / 328 (8.23%)		
occurrences (all)	43		
Infections and infestations			

covid-19 alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences (all) nasopharyngitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences (all)	 12 / 328 (3.66%) 12 16 / 328 (4.88%) 17		
Metabolism and nutrition disorders decreased appetite alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences (all)	 36 / 328 (10.98%) 46		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 July 2020	Amendment (b): Added final treatment visit and corresponding activities, added language regarding the final treatment visit, added language for safety interim analysis and added language describing changes to the study procedures due to the COVID-19 pandemic.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported