Clinical trial results:
A Phase 3, Multicenter, Randomized, Parallel-Design, Open-Label Trial to Evaluate the Efficacy and Safety of LY3209590 Compared with Insulin Degludec in Participants with Type 2 Diabetes Currently Treated with Basal Insulin (QWINT-3)

Summary

EudraCT number	2021-002569-16
Trial protocol	SK HU ES PL
Global end of trial date	15 May 2024

Results information

Result version number	v1 (current)
This version publication date	31 May 2025
First version publication date	31 May 2025

Trial information

Trial identification

Sponsor protocol code	I8H-MC-BDCU

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05275400
WHO universal trial number (UTN)	-

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,, Eli Lilly, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, , Eli Lilly, 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	15 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the hypothesis that LY3209590 is noninferior to the comparator (insulin degludec) on glycemic control in study participants with T2D currently on basal insulin

Protection of trial subjects:

his 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	08 March 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 88
Country: Number of subjects enrolled	Slovakia: 91
Country: Number of subjects enrolled	Spain: 77
Country: Number of subjects enrolled	Hungary: 38
Country: Number of subjects enrolled	Argentina: 155
Country: Number of subjects enrolled	Japan: 141
Country: Number of subjects enrolled	Korea, Republic of: 95
Country: Number of subjects enrolled	Taiwan: 30
Country: Number of subjects enrolled	United States: 271
Worldwide total number of subjects	986
EEA total number of subjects	294

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)	602
From 65 to 84 years	383
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants underwent a 3 week screening and lead-in period, and a 78-week treatment period, followed by a 5-week safety follow-up period.

Pre-assignment

Screening details:

NA

Period 1

Period 1 title	Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	500 U/mL - Insulin Efsitora

Arm description:

Participants received 500 units per milliliter (U/mL) Insulin Efsitora Alfa (insulin efsitora) administered subcutaneously (SC) once weekly (QW).

Arm type	Experimental
Investigational medicinal product name	Insulin Efsitora
Investigational medicinal product code	
Other name	LY3209590
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered subcutaneously.

Arm title	100 U/mL - Insulin Degludec

Arm description:

Participants received 100 U/mL insulin degludec administered SC once daily (QD).

Arm type	Active comparator
Investigational medicinal product name	Insulin Degludec
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered subcutaneously.

Number of subjects in period 1	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec
Started	655	331
Received At Least 1 Dose of Study Drug	655	331
Completed	593	303
Not completed	62	28
Physician decision	5	4
Consent withdrawn by subject	30	12
Non-Compliance with Study Drug	5	1
Adverse event, non-fatal	7	1
Death	5	2
Sponsor Decision	1	-
Lost to follow-up	1	5
Assigned Treatment by Mistake	6	3
Protocol deviation	1	-
Lack of efficacy	1	-

Period 2

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

Arms

Are arms mutually exclusive?	No
Arm title	500 U/mL - Insulin Efsitora

Arm description:

Participants received 500 units per milliliter (U/mL) Insulin Efsitora Alfa (insulin efsitora) administered subcutaneously (SC) once weekly (QW).

Arm type	Experimental
Investigational medicinal product name	Insulin Efsitora
Investigational medicinal product code	
Other name	LY3209590
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered subcutaneously.

Arm title	100 U/mL - Insulin Degludec

Arm description:

Participants received 100 U/mL insulin degludec administered SC once daily (QD).

Arm type	Active comparator

Investigational medicinal product name	Insulin Degludec
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered subcutaneously.

Number of subjects in period 2	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec
Started	614	306
Completed	608	306
Not completed	6	0
Consent withdrawn by subject	3	-
Death	2	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	500 U/mL - Insulin Efsitora
Reporting group description:	
Participants received 500 units per milliliter (U/mL) Insulin Efsitora Alfa (insulin efsitora) administered subcutaneously (SC) once weekly (QW).	
Reporting group title	100 U/mL - Insulin Degludec
Reporting group description:	
Participants received 100 U/mL insulin degludec administered SC once daily (QD).	

Reporting group values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec	Total
Number of subjects	655	331	986
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	407	195	602
From 65-84 years	247	136	383
85 years and over	1	0	1
Gender categorical Units: Subjects			
Female	279	152	431
Male	376	179	555
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	179	88	267
Not Hispanic or Latino	476	243	719
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	0	2
Asian	180	92	272
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	32	20	52
White	438	218	656
More than one race	2	1	3
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Argentina	103	52	155
Hungary	24	14	38
Poland	59	29	88

Slovakia	60	31	91
South Korea	64	31	95
Spain	52	25	77
Taiwan	19	11	30
United States	180	91	271
Japan	94	47	141

End points

End points reporting groups

Reporting group title	500 U/mL - Insulin Efsitora
Reporting group description:	
Participants received 500 units per milliliter (U/mL) Insulin Efsitora Alfa (insulin efsitora) administered subcutaneously (SC) once weekly (QW).	
Reporting group title	100 U/mL - Insulin Degludec
Reporting group description:	
Participants received 100 U/mL insulin degludec administered SC once daily (QD).	
Reporting group title	500 U/mL - Insulin Efsitora
Reporting group description:	
Participants received 500 units per milliliter (U/mL) Insulin Efsitora Alfa (insulin efsitora) administered subcutaneously (SC) once weekly (QW).	
Reporting group title	100 U/mL - Insulin Degludec
Reporting group description:	
Participants received 100 U/mL insulin degludec administered SC once daily (QD).	

Primary: Change From Baseline in Hemoglobin A1c (HbA1c) [Noninferiority]

End point title	Change From Baseline in Hemoglobin A1c (HbA1c) [Noninferiority]
End point description:	
HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time. Least Squares (LS) Mean was determined using ANCOVA model with Baseline + Country + Type of Basal Insulin used at Baseline + Treatment (Type III sum of squares) as variables. Missing data at Week 26 were imputed by return-to-baseline multiple imputation approach. Analysis Population Description (APD): All participants who received at least one dose of study drug and had evaluable data for this outcome at baseline or week 26. Participants who were assigned treatment by mistake were excluded.	
End point type	Primary
End point timeframe:	
Baseline, Week 26	

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	649	328		
Units: Percentage of HbA1c				
least squares mean (standard error)	-0.81 (± 0.0302)	-0.72 (± 0.0424)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 1
Statistical analysis description: Noninferiority margin (NIM) was 0.4%	
Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec
Number of subjects included in analysis	977
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	LS Mean Difference
Point estimate	-0.089
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.191
upper limit	0.013

Secondary: Nocturnal Hypoglycemia Event Rate

End point title	Nocturnal Hypoglycemia Event Rate
End point description: The event rate of participant-reported clinically significant glucose <54 mg/dL (3.0 mmol/L) or severe nocturnal hypoglycemia that occurs at night and presumably during sleep between midnight and 6:00 AM), measured during treatment period up to week 78. Group mean is reported here. Group mean is determined by Negative Binomial Model using Number of episodes = Hemoglobin A1c at Baseline (%) + Treatment, with log (exposure in days/365.25) as an offset variable. APD: All participants who received at least one dose of study drug.	
End point type	Secondary
End point timeframe: Baseline up to Week 78	

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	655	331		
Units: Events per year				
arithmetic mean (standard error)	0.11 (± 0.022)	0.10 (± 0.019)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 2
Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec

Number of subjects included in analysis	986
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.897
Method	Negative Binomial Model
Parameter estimate	Relative Rate
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.74

Secondary: Percentage of Time in Glucose Range

End point title	Percentage of Time in Glucose Range

End point description:

Percentage of time in glucose range between 70 and 180 mg/dL (3.9 and 10.0 millimoles per liter (mmol/L)) inclusive measured by continued glucose monitoring (CGM) during CGM session prior to week 26. LS Mean was calculated using ANCOVA model with Baseline + Country + Hemoglobin A1c Stratum at Baseline + Type of Basal Insulin used at Baseline + Treatment (Type III sum of squares) as variables. Missing data during CGM session prior to Week 26 were imputed by return-to-baseline multiple imputation approach.

APD: All randomized participants who took at least one dose of the study drug and had evaluable data for this outcome at baseline or Week 22-26 were included. Participants who were assigned treatment by mistake were excluded.

End point type	Secondary

End point timeframe:

Week 22 to Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	641	325		
Units: Percentage of time				
least squares mean (standard error)	61.37 (± 0.676)	60.95 (± 0.954)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 3
Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec

Number of subjects included in analysis	966
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.722
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.88
upper limit	2.72

Secondary: Change From Baseline in Fasting Glucose

End point title	Change From Baseline in Fasting Glucose

End point description:

Fasting glucose measured by Self-Monitoring of Blood Glucose (SMBG). LS Mean was determined using ANCOVA model with Baseline + Country + Type of Basal Insulin at Baseline + Baseline HbA1C Stratum (%) + Treatment (Type III sum of squares) as variables. Missing data at baseline are imputed with multiple imputation under assumption of missing at random. Missing data at Week 26 are imputed by return-to-baseline multiple imputation approach.

APD: All randomized participants who took at least one dose of the study drug and had evaluable data for this outcome at baseline or Week 26 were included. Participants who were assigned treatment by mistake were excluded.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	648	327		
Units: milligrams per deciliter (mg/dL)				
least squares mean (standard error)	-30.97 (± 0.943)	-30.13 (± 1.323)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 4
Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec

Number of subjects included in analysis	975
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.605
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.01
upper limit	2.33

Secondary: Weekly Insulin Dose at Week 26

End point title	Weekly Insulin Dose at Week 26

End point description:

The average weekly insulin dose at Week 26 was reported. LS Mean was determined by mixed model repeated measures (MMRM) model using BASELINE + Country + Type of Basal Insulin at Baseline + Baseline HbA1C Stratum (%) + Treatment + Time + Treatment*Time (Type III sum of squares) as variables. Variance-covariance structure was set as compound symmetry.

APD: All participants who received at least one dose of study drug, had a baseline and at least one post-baseline value for this outcome. Participants who were assigned treatment by mistake were excluded.

End point type	Secondary

End point timeframe:

Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	647	327		
Units: Units per week of insulin				
least squares mean (standard error)	333.20 (± 5.93)	363.20 (± 8.33)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 5
Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec

Number of subjects included in analysis	974
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-30
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.1
upper limit	-9.97

Secondary: Hypoglycemia Event Rate

End point title	Hypoglycemia Event Rate

End point description:

Patient reported events of hypoglycemia - Hypoglycemia with glucose <54 mg/dL (Level 2) or Severe Hypoglycemia (Level 3) was reported. A severe hypoglycemic event is characterized by altered mental or physical status requiring assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions for the treatment of hypoglycemia. Group mean was reported and determined by Negative binomial method using Hemoglobin A1c at Baseline (%) + Treatment, with log (exposure in days/365.25) as variables.

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

End point type	Secondary

End point timeframe:

Baseline up to Week 78

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	655	331		
Units: Events per year				
arithmetic mean (standard error)	0.84 (± 0.082)	0.74 (± 0.098)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 6
Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec

Number of subjects included in analysis	986
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.43
Method	Negative Binomial Model
Parameter estimate	Relative Rate
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.56

Secondary: Change From Baseline in Body Weight

End point title	Change From Baseline in Body Weight

End point description:

Change from baseline in body weight was reported. LS Mean was determined by MMRM model using BASELINE + Treatment + Time + Treatment*Time (Type III sum of squares) as variables.

APD: All participants who received at least one dose of study drug, had a baseline and at least one post-baseline value for this outcome. Participants who were assigned treatment by mistake were excluded.

End point type	Secondary

End point timeframe:

Baseline, Week 78

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	654	330		
Units: Kilograms (kg)				
least squares mean (standard error)	2.27 (± 0.133)	2.20 (± 0.186)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 7
Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec
Number of subjects included in analysis	984
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.756
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.071

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	0.52

Secondary: Percentage of Time in Hypoglycemia Range

End point title	Percentage of Time in Hypoglycemia Range

End point description:

Percentage of time in hypoglycemia range with glucose <54 mg/dL (3.0 mmol/L) measured during CGM from 22-26 weeks. LS Mean was determined using ANCOVA model using Baseline + Country + Hemoglobin A1c Stratum at Baseline + Type of Basal Insulin used at Baseline + Treatment (Type III sum of squares) as variables. Missing data at baseline were imputed with multiple imputation under assumption of missing at random. Missing data at Week 22-26 were imputed by return-to-baseline multiple imputation approach.

APD: All randomized participants who took at least one dose of the study drug and had evaluable data for this outcome at baseline or Week 22-26 were included. Participants who were assigned treatment by mistake were excluded.

End point type	Secondary

End point timeframe:

Week 22 to Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	641	325		
Units: Percentage of time				
least squares mean (standard error)	0.36 (± 0.036)	0.22 (± 0.051)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 8
Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec
Number of subjects included in analysis	966
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.27

Secondary: Percentage of Time in Hyperglycemia Range

End point title	Percentage of Time in Hyperglycemia Range

End point description:

Percentage of time in hyperglycemia range with glucose >180 mg/dL (10.0 mmol/L) measured during the CGM session from 22-26 weeks. LS Mean was determined using ANCOVA model using Baseline + Country + Hemoglobin A1c Stratum at Baseline + Type of Basal Insulin used at Baseline + Treatment (Type III sum of squares) as variables. Missing data at baseline were imputed with multiple imputation under assumption of missing at random. Missing data at Week 22-26 were imputed by return-to-baseline multiple imputation approach.

APD: All randomized participants who took at least one dose of the study drug and had evaluable data for this outcome at baseline or Week 22-26 were included. Participants who were assigned treatment by mistake were excluded.

End point type	Secondary

End point timeframe:

Week 22 to Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	641	325		
Units: Percentage of time				
least squares mean (standard error)	37.25 (± 0.700)	38.24 (± 0.989)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 9
Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec
Number of subjects included in analysis	966
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.417
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.37
upper limit	1.4

Secondary: Change From Baseline in Treatment-Related Impact Measure - Diabetes (TRIM-D)

End point title	Change From Baseline in Treatment-Related Impact Measure - Diabetes (TRIM-D)

End point description:

The TRIM-D is a self-administered instrument, which assesses the impact of diabetes treatment on participants' functioning and well-being across available diabetes treatments. The TRIM-D consists of 28 items each assessed on a 5-point scale. TRIM-D items assess 5 domains of impact:
- Treatment Burden (6 items)
- Daily Life (5 items)
- Diabetes Management (5 items)
- Compliance (4 items), and
- Psychological Health (8 items)

Items within each domain are summed to obtain a raw domain score, which is then transformed to a 0-100 scale, where higher scores indicate a greater impact on participant's functioning and well-being.

LS mean was determined using MMRM model with BASELINE + Country + Type of Basal Insulin at Baseline + Baseline HbA1C Stratum (%) + Treatment + Time + Treatment*Time (Type III sum of squares) as variables.

End point type	Secondary

End point timeframe:

Baseline, Week 26, Week 52, Week 78

APD: All participants who received at least one dose of the study drug, had a baseline and at least one post-baseline value for this outcome. Participants who were assigned treatment by mistake were excluded.

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	625[1]	314[2]		
Units: Score on a scale				
least squares mean (standard error)				
Week 26	10.03 (± 0.424)	6.88 (± 0.599)		
Week 52	10.09 (± 0.445)	6.53 (± 0.627)		
Week 78	10.33 (± 0.472)	6.98 (± 0.662)		

Notes:

[1] - For Week 26: n = 625; For Week 52: n = 580; For Week 78: n = 548.

[2] - For Week 26: n = 314; For Week 52: n = 294; For Week 78: n = 281.

Statistical analyses

Statistical analysis title	Outcome Measure No. 10 - Week 26

Statistical analysis description:

For Week 26: LS Mean was determined using MMRM model with BASELINE + Country + Type of Basal Insulin at Baseline + Baseline HbA1C Stratum (%) + Treatment + Time + Treatment*Time (Type III sum of squares) as variables.

Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec

Number of subjects included in analysis	939
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	3.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.71
upper limit	4.59

Statistical analysis title	Outcome Measure No. 10 - Week 52

Statistical analysis description:

For Week 52: LS Mean was determined by MMRM model using BASELINE + Country + Type of Basal Insulin at Baseline + Baseline HbA1C Stratum (%) + Treatment + Time + Treatment*Time (Type III sum of squares) as variables.
Subjects in this analysis: 874

Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec
Number of subjects included in analysis	939
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	3.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.05
upper limit	5.07

Statistical analysis title	Outcome Measure No. 10 - Week 78

Statistical analysis description:

For Week 78: LS Mean was determined by MMRM model using BASELINE + Country + Type of Basal Insulin at Baseline + Baseline HbA1C Stratum (%) + Treatment + Time + Treatment*Time (Type III sum of squares) as variables.
Subjects in this analysis: 829

Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec
Number of subjects included in analysis	939
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	3.35

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.75
upper limit	4.94

Secondary: Diabetes Treatment Satisfaction Questionnaire-Change Version (DTSQc) - Treatment Satisfaction Score: Week 26

End point title	Diabetes Treatment Satisfaction Questionnaire-Change Version (DTSQc) - Treatment Satisfaction Score: Week 26

End point description:

DTSQc treatment satisfaction score is a 6-item questionnaire which assesses relative change in overall treatment satisfaction. The treatment satisfaction score ranges from -18 to 18, where higher the score the greater the improvement in satisfaction with treatment. The lower the score the greater the deterioration in satisfaction with treatment.

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome. Participants who were assigned treatment by mistake were excluded.

End point type	Secondary

End point timeframe:

Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	599	304		
Units: Score on a scale				
arithmetic mean (standard deviation)	14.9 (± 4.47)	12.3 (± 6.15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Diabetes Treatment Satisfaction Questionnaire-Change Version (DTSQc) - Treatment Satisfaction Score: Week 52

End point title	Diabetes Treatment Satisfaction Questionnaire-Change Version (DTSQc) - Treatment Satisfaction Score: Week 52

End point description:

DTSQc treatment satisfaction score is a 6-item questionnaire which assesses relative change in overall treatment satisfaction. The treatment satisfaction score ranges from -18 to 18, where higher the score the greater the improvement in satisfaction with treatment. The lower the score the greater the deterioration in satisfaction with treatment.

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome. Participants who were assigned treatment by mistake were excluded.

End point type	Secondary

End point timeframe:

Week 52

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	570	290		
Units: Score on a scale				
arithmetic mean (standard deviation)	15.1 (± 4.45)	12.3 (± 6.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Diabetes Treatment Satisfaction Questionnaire-Change Version (DTSQc) - Treatment Satisfaction Score: Week 78

End point title	Diabetes Treatment Satisfaction Questionnaire-Change Version (DTSQc) - Treatment Satisfaction Score: Week 78

End point description:

DTSQc treatment satisfaction score is a 6-item questionnaire which assesses relative change in overall treatment satisfaction. The treatment satisfaction score ranges from -18 to 18, where higher the score the greater the improvement in satisfaction with treatment. The lower the score the greater the deterioration in satisfaction with treatment.

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome. Participants who were assigned treatment by mistake were excluded.

End point type	Secondary

End point timeframe:

Week 78

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	523	268		
Units: Score on a scale				
arithmetic mean (standard deviation)	15.4 (± 4.23)	11.7 (± 6.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hemoglobin A1c (HbA1c) [Superiority]

End point title	Change From Baseline in Hemoglobin A1c (HbA1c) [Superiority]

End point description:

HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time. Least Squares (LS) Mean was determined using ANCOVA model with Baseline + Country + Type of Basal Insulin used at Baseline + Treatment (Type III sum of squares) as variables. Missing data at Week 26 were imputed by return-to-baseline multiple imputation approach.

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome at baseline or week 26. Participants who were assigned treatment by mistake were excluded.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	649	328		
Units: Percentage of HbA1c				
least squares mean (standard error)	-0.81 (± 0.0302)	-0.72 (± 0.0424)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 14
Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Degludec
Number of subjects included in analysis	977
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.088
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.089
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.191
upper limit	0.013

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline Through Safety Follow-Up (Up to 83 Weeks)	
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	27.0

Reporting groups	
Reporting group title	500 U/mL - Insulin Efsitora
Reporting group description:	
Participants received 500 U/mL insulin efsitora administered SC QW.	
Reporting group title	100 U/mL - Insulin Degludec
Reporting group description:	
Participants received 100 U/mL insulin degludec administered SC QD.	

Serious adverse events	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec	
Total subjects affected by serious adverse events			
subjects affected / exposed	103 / 655 (15.73%)	37 / 331 (11.18%)	
number of deaths (all causes)	7	2	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
angiomyolipoma			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
carcinoid tumour pulmonary			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
chromophobe renal cell carcinoma			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
chronic lymphocytic leukaemia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
colorectal adenocarcinoma			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ductal adenocarcinoma of pancreas			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
endometrial adenocarcinoma			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed[1]	0 / 279 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastric cancer			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastrointestinal stromal tumour			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

malignant melanoma in situ			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
metastases to meninges			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
metastatic gastric cancer			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
prostate cancer			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed[2]	4 / 376 (1.06%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
salivary gland cancer			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
small cell lung cancer metastatic			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
transitional cell carcinoma			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
aortic stenosis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
aneurysm thrombosis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
arterial disorder			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
deep vein thrombosis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
extremity necrosis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 655 (0.31%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
peripheral arterial occlusive disease			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	2 / 655 (0.31%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
peripheral artery stenosis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
peripheral ischaemia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
shock haemorrhagic			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
coronary revascularisation			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 655 (0.31%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
limb amputation			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
skin graft			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
death			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
chest pain			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
multiple organ dysfunction syndrome			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
sudden death			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
vascular stent stenosis			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
benign prostatic hyperplasia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed[3]	1 / 376 (0.27%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pelvic pain			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
acute respiratory failure			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
atelectasis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
asthma			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bronchiectasis			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
cough			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dyspnoea			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary embolism			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 655 (0.31%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
vocal cord polyp			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
continuous glucose monitoring			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
craniofacial fracture			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
fall			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
foot fracture			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
fractured sacrum			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
head injury			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
humerus fracture			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
incorrect dose administered			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ligament rupture			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
limb crushing injury			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hip fracture			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pelvic fracture			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

radius fracture			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
rib fracture			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
road traffic accident			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal compression fracture			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
tibia fracture			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
wound			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
phimosis			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed[4]	1 / 376 (0.27%)	0 / 179 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	4 / 655 (0.61%)	4 / 331 (1.21%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
acute left ventricular failure			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
arrhythmia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
angina unstable			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	5 / 655 (0.76%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
angina pectoris			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
arteriosclerosis coronary artery			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrioventricular block complete			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrial flutter			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrial fibrillation			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac failure			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	3 / 655 (0.46%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
cardiogenic shock			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
cardio-respiratory arrest			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

cardiac valve disease			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac failure chronic			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 655 (0.31%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
chronic coronary syndrome			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
coronary artery disease			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	4 / 331 (1.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
coronary artery stenosis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
left ventricular dysfunction			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
microvascular coronary artery disease			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocardial infarction			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 655 (0.31%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
ventricular extrasystoles			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
carotid artery stenosis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebral infarction			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 655 (0.31%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebrovascular accident			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dural arteriovenous fistula			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
headache			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hemiplegia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoglycaemic unconsciousness			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 655 (0.31%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ischaemic stroke			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
lacunar infarction			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
metabolic encephalopathy			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

myelopathy			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spondylitic myelopathy			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
thalamus haemorrhage			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
vertigo positional			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
cataract			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	3 / 655 (0.46%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
diabetic retinopathy			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 655 (0.31%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diplopia			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
retinal detachment			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 655 (0.31%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
abdominal adhesions			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
abdominal pain upper			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
abdominal pain			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
alcoholic pancreatitis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastritis			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
inguinal hernia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
inguinal hernia, obstructive			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancreatitis acute			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
acute cholecystitis necrotic			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholecystitis acute			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholelithiasis			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hepatitis acute			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypertransaminasaemia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
diabetic foot			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
calculus bladder			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bladder neck obstruction			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
haematuria			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
nephrolithiasis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 655 (0.31%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ureteric stenosis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
primary hyperthyroidism			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
arthritis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
back pain			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
intervertebral disc protrusion			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
osteoarthritis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
lumbar spinal stenosis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal osteoarthritis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
spondylolisthesis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 655 (0.31%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
abscess limb			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
appendicitis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
covid-19 pneumonia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	2 / 655 (0.31%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
covid-19			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bronchitis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	2 / 331 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
cytomegalovirus infection			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
gangrene			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

gastroenteritis viral			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hcov-oc43 infection			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hiv infection			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
localised infection			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
infective exacerbation of asthma			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
intervertebral discitis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lower respiratory tract infection			
alternative dictionary used: MedDRA 27.0			

subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
perirectal abscess			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
osteomyelitis			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	3 / 655 (0.46%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	3 / 655 (0.46%)	4 / 331 (1.21%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
septic shock			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
pneumocystis jirovecii infection			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	1 / 655 (0.15%)	0 / 331 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper respiratory tract infection			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

urinary tract infection			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	0 / 655 (0.00%)	1 / 331 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
hypoglycaemia			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	4 / 655 (0.61%)	2 / 331 (0.60%)	
occurrences causally related to treatment / all	4 / 5	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk 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: Gender specific events occurring only in male or female participants have had the number of participants at risk 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: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.

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

Non-serious adverse events	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Degludec	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	241 / 655 (36.79%)	102 / 331 (30.82%)	
Injury, poisoning and procedural complications			
dose calculation error			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	42 / 655 (6.41%)	15 / 331 (4.53%)	
occurrences (all)	55	18	
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 27.0			
subjects affected / exposed	36 / 655 (5.50%)	7 / 331 (2.11%)	
occurrences (all)	57	9	

Gastrointestinal disorders diarrhoea alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences (all)	 35 / 655 (5.34%) 46	 14 / 331 (4.23%) 23	
Musculoskeletal and connective tissue disorders arthralgia alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences (all) back pain alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences (all)	 34 / 655 (5.19%) 39 33 / 655 (5.04%) 35	 12 / 331 (3.63%) 13 12 / 331 (3.63%) 12	
Infections and infestations covid-19 alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences (all) upper respiratory tract infection alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences (all) nasopharyngitis alternative dictionary used: MedDRA 27.0 subjects affected / exposed occurrences (all)	 70 / 655 (10.69%) 73 34 / 655 (5.19%) 40 60 / 655 (9.16%) 88	 27 / 331 (8.16%) 28 18 / 331 (5.44%) 25 29 / 331 (8.76%) 36	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 May 2022	- Changes made to address regulatory feedback regarding exclusionary ALT and AST thresholds and include specific details for participants who enter the study and use personal CGM.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported