Clinical trial results:
A Phase 3, Parallel-Design, Open-Label, Randomized Controlled Study to Evaluate the Efficacy and Safety of LY3209590 as a Weekly Basal Insulin Compared to Insulin Glargine in Adults with Type 2 Diabetes on Multiple Daily Injections

Summary

EudraCT number	2021-005878-25
Trial protocol	DE ES IT
Global end of trial date	27 February 2024

Results information

Result version number	v1 (current)
This version publication date	15 March 2025
First version publication date	15 March 2025

Trial information

Trial identification

Sponsor protocol code	I8H-MC-BDCV

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05462756
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 18260

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	27 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The reason for this study is to evaluate if the once-weekly study drug insulin efsitora alfa (LY3209590) is safe and effective compared with daily insulin glargine in participants with Type 2 diabetes (T2D) that have already been treated with basal insulin and at least 2 injections per day of prandial insulin. The study consists of a 3-week screening/lead-in period, a 26-week treatment period and a 5-week safety follow-up period. The study will last up to 34 weeks.

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	11 August 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	Argentina: 166
Country: Number of subjects enrolled	Germany: 51
Country: Number of subjects enrolled	India: 100
Country: Number of subjects enrolled	Italy: 26
Country: Number of subjects enrolled	Mexico: 169
Country: Number of subjects enrolled	Spain: 70
Country: Number of subjects enrolled	United States: 148
Worldwide total number of subjects	730
EEA total number of subjects	147

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)	508
From 65 to 84 years	220
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Participants underwent a 26-week treatment period, followed by a 5-week safety follow-up period.

Pre-assignment

Screening details:

Not Applicable

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) along with 100 U/mL insulin lispro given SC.

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 Glargine

Arm description:

Participants received 100 U/mL insulin glargine administered SC once daily (QD) along with 100 U/mL insulin lispro given SC.

Arm type	Active comparator
Investigational medicinal product name	Insulin Glargine
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 Glargine
Started	365	365
Received At Least 1 Dose of Study Drug	365	365
Completed	348	344
Not completed	17	21
Physician decision	2	-
Consent withdrawn by subject	5	12
Non-Compliance with Study Drug	1	3
Adverse event, non-fatal	3	-
Death	-	1
Lost to follow-up	2	1
Assigned Treatment by Mistake	4	3
Protocol deviation	-	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 who received 500 U/mL insulin efsitora administered SC QW along with 100 U/mL insulin lispro given SC in the treatment period were required to complete a safety follow-up period and participants who discontinued the study treatment prematurely were encouraged to remain in the study for safety monitoring.

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 Glargine

Arm description:

Participants who received 100 U/mL insulin glargine administered SC once daily (QD) along with 100 U/mL insulin lispro given SC in the treatment period were required to complete a safety follow-up period and participants who discontinued the study treatment prematurely were encouraged to remain in the study for safety monitoring.

Arm type	Active comparator

Investigational medicinal product name	Insulin Glargine
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 Glargine
Started	357	354
Completed	352	349
Not completed	5	5
Consent withdrawn by subject	-	4
Adverse event, non-fatal	1	-
Death	1	-
Lost to follow-up	3	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) along with 100 U/mL insulin lispro given SC.	
Reporting group title	100 U/mL - Insulin Glargine
Reporting group description:	
Participants received 100 U/mL insulin glargine administered SC once daily (QD) along with 100 U/mL insulin lispro given SC.	

Reporting group values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine	Total
Number of subjects	365	365	730
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)	265	243	508
From 65-84 years	99	121	220
85 years and over	1	1	2
Gender categorical Units: Subjects			
Female	193	176	369
Male	172	189	361
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	201	203	404
Not Hispanic or Latino	163	161	324
Unknown or Not Reported	1	1	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	46	45	91
Asian	54	51	105
Black or African American	20	11	31
White	245	258	503
Region of Enrollment Units: Subjects			
Argentina	83	83	166
Germany	27	24	51
India	50	50	100
Italy	11	15	26
Mexico	85	84	169
Spain	35	35	70

United States	74	74	148

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) along with 100 U/mL insulin lispro given SC.	
Reporting group title	100 U/mL - Insulin Glargine
Reporting group description:	
Participants received 100 U/mL insulin glargine administered SC once daily (QD) along with 100 U/mL insulin lispro given SC.	
Reporting group title	500 U/mL - Insulin Efsitora
Reporting group description:	
Participants who received 500 U/mL insulin efsitora administered SC QW along with 100 U/mL insulin lispro given SC in the treatment period were required to complete a safety follow-up period and participants who discontinued the study treatment prematurely were encouraged to remain in the study for safety monitoring.	
Reporting group title	100 U/mL - Insulin Glargine
Reporting group description:	
Participants who received 100 U/mL insulin glargine administered SC once daily (QD) along with 100 U/mL insulin lispro given SC in the treatment period were required to complete a safety follow-up period and participants who discontinued the study treatment prematurely were encouraged to remain in the study for safety monitoring.	

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. Analysis Population Description (APD): All participants who received at least one dose of study drug and had at least one post-baseline HbA1c data.	
End point type	Primary
End point timeframe:	
Baseline, Week 26	

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	362		
Units: millimoles per mole (mmol/mol)				
least squares mean (standard error)	-11.09 (± 0.506)	-10.95 (± 0.506)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 1

Statistical analysis description:

Least Squares (LS) Mean was determined using ANCOVA model with Baseline + Country + Personal Use of CGM or FGM at Randomization + Treatment (Type III sum of squares) as variables. Missing data at Week 26 were imputed by return-to-baseline multiple imputations approach. A total of 100 datasets were imputed. The NIM of 0.4% is equivalent to a NIM of 4.372 mmol/mol.

Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Glargine
Number of subjects included in analysis	723
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	LS Mean Difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.534
upper limit	1.272

Notes:

[1] - The sample size provided >99% statistical power to show noninferiority assuming a 0.4% noninferiority margin (NIM), in insulin efsitora doses compared to insulin glargine, in a 1:1 randomization, a standard deviation (SD) of 1.1%, and a dropout rate of 15%.

Secondary: Change From Baseline in HbA1c [Superiority]

End point title	Change From Baseline in 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.

APD: All participants who received at least one dose of study drug and had at least one post-baseline HbA1c data.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	362		
Units: millimoles per mole				
least squares mean (standard error)	-11.09 (± 0.506)	-10.95 (± 0.506)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 2

Statistical analysis description:

Least Squares (LS) Mean was determined using ANCOVA model with Baseline + Country + Personal Use of CGM or FGM at Randomization + Treatment (Type III sum of squares) as variables. Missing data at Week 26 were imputed by return-to-baseline multiple imputations approach. A total of 100 datasets were imputed.

Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Glargine
Number of subjects included in analysis	723
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.855
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.534
upper limit	1.272

Secondary: Percentage of Participants Achieving HbA1c <7% Without Nocturnal Hypoglycemia

End point title	Percentage of Participants Achieving HbA1c <7% Without Nocturnal Hypoglycemia

End point description:

Percentage of participants achieving HbA1c <7% without nocturnal hypoglycemia [<54 milligram/deciliter (mg/dL) 3.0 millimole/Liter (mmol/L)] or severe during treatment phase up to week 26. Nocturnal hypoglycemia is a hypoglycemia event, including severe hypoglycemia, that occurs at night and presumably during sleep between midnight and 6:00 am.

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	362		
Units: Percentage of participants				
number (not applicable)	38.6	35.9		

Statistical analyses

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

Number of subjects included in analysis	723
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.504
Method	Chi-squared
Parameter estimate	Odds ratio (OR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.52

Secondary: Nocturnal Hypoglycemia Event Rate

End point title	Nocturnal Hypoglycemia Event Rate

End point description:

The event rate of participant-reported clinically significant nocturnal hypoglycemia, (where glucose <54 mg/dL (3.0 mmol/L) or severe and occurs at night and presumably during sleep between midnight and 6:00 am), measured during treatment phase up to week 26.

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Baseline Up To Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	365	365		
Units: Events per year				
arithmetic mean (standard error)	0.67 (± 0.112)	1.00 (± 0.151)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 4

Statistical analysis description:

Group mean is determined by Negative Binomial Model using Number of episodes = Baseline hypoglycemia rate + Hemoglobin A1c at Baseline (%) + Treatment, with log (exposure in days/365.25) as an offset variable.

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

Number of subjects included in analysis	730
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.058
Method	Negative binomial model
Parameter estimate	Relative Rate
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	1.01

Secondary: Change From Baseline in Fasting Glucose

End point title	Change From Baseline in Fasting Glucose

End point description:

Change from baseline in fasting glucose measured by self-monitoring blood glucose (SMBG).

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	361		
Units: millimoles per liter				
least squares mean (standard error)	-1.71 (± 0.104)	-1.48 (± 0.104)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 5

Statistical analysis description:

LS Mean was determined using ANCOVA model using Baseline + Country + Personal Use of CGM or FGM at Randomization + Hemoglobin A1c Stratum at Baseline + Treatment (Type III sum of squares) as variables. Missing data at Baseline were imputed with multiple imputation with assumption of missing at random. Missing data at Week 26 were imputed by return-to-baseline multiple imputations approach. A total of 100 datasets were imputed with one for each of the 100 datasets imputed at Baseline.

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

Number of subjects included in analysis	722
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.104
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.525
upper limit	0.049

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 mmol/L), inclusive measured during the continuous glucose monitoring (CGM) session.

APD: All participants who received at least one dose of the study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Week 22 to Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359	360		
Units: Percentage of time				
least squares mean (standard error)	58.39 (± 0.993)	57.05 (± 0.990)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 6

Statistical analysis description:

LS Mean was determined using ANCOVA model using Baseline + Country + Personal Use of CGM or FGM at Randomization + Hemoglobin A1c Stratum at Baseline + Treatment (Type III sum of squares) as variables. Missing data at Baseline were imputed with multiple imputation with assumption of missing at random. Missing data at Week 22-Week 26 were imputed by return-to-baseline multiple imputations approach. A total of 100 datasets were imputed with one for each of the 100 datasets imputed at Baseline.

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

Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.337
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.404
upper limit	4.101

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 by CGM.

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Week 22 to Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359	360		
Units: Percentage of time				
least squares mean (standard error)	6.84 (± 0.700)	5.25 (± 0.680)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 7

Statistical analysis description:

LS Mean was determined by ANCOVA model using Baseline + Country + Personal Use of CGM or FGM at Randomization + Hemoglobin A1c Stratum at Baseline + Treatment (Type III sum of squares) as variables. Missing data at Baseline were imputed with multiple imputation with assumption of missing at random. Missing data at Week 22-Week 26 were imputed by return-to-baseline multiple imputations approach. A total of 100 datasets were imputed with one for each of the 100 datasets imputed at Baseline.

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

Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.104
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.327
upper limit	3.508

Secondary: Percentatge of Time in Hyperglycemia Range

End point title	Percentatge of Time in Hyperglycemia Range

End point description:

Percentage of Time in hyperglycemia range with glucose >180 mg/dL (10.0 mmol/L), measured by CGM.

End point type	Secondary

End point timeframe:

Week 22 to Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	359	360		
Units: Percentage of time				
least squares mean (standard error)	40.10 (± 1.024)	41.60 (± 1.024)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 8

Statistical analysis description:

LS Mean was determined by ANCOVA model using Baseline + Country + Personal Use of CGM or FGM at Randomization + Hemoglobin A1c Stratum at Baseline + Treatment (Type III sum of squares). Missing data at Baseline were imputed with multiple imputation with assumption of missing at random. Missing data at Week 22-Week 26 were imputed by return-to-baseline multiple imputations approach. A total of 100 datasets were imputed with one for each of the 100 datasets imputed at Baseline.

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

Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.304
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.358
upper limit	1.36

Secondary: Glucose Variability Between Weeks 22 to 26

End point title	Glucose Variability Between Weeks 22 to 26

End point description:

Glucose variability measured as coefficient of variation for glucose within day for 24-hour period between Week 22 and 26 was reported.

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Week 22 to Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	334	341		
Units: Coefficient of Variation				
least squares mean (standard error)	28.51 (± 0.259)	28.28 (± 0.254)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 9

Statistical analysis description:

LS Mean was determined by MMRM model with BASELINE + Hemoglobin A1c Stratum at Baseline + Country + Personal Use CGM or FGM at Randomization + Treatment + Time + Treatment*Time (Type III sum of squares) as variables. Unstructured variance-covariance structure was used.

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

Number of subjects included in analysis	675
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.523
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.95

Secondary: Basal Insulin Dose at Week 26

End point title	Basal Insulin Dose at Week 26

End point description:

Average weekly basal Insulin Dose at Week 26 was reported.

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	360	362		
Units: Units per week of basal insulin				
least squares mean (standard error)	391.59 (± 7.482)	426.62 (± 7.323)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 10

Statistical analysis description:

LS Mean was determined by Mixed Model Repeated Measures (MMRM) model using BASELINE + Hemoglobin A1c Stratum at Baseline + Country + Personal Use CGM or FGM at Randomization + Treatment + Time + Treatment*Time (Type III sum of squares) as variables. Variance-covariance structure was set as compound symmetry.

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

Number of subjects included in analysis	722
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-35.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.57
upper limit	-14.5

Secondary: Bolus Insulin Dose at Week 26

End point title	Bolus Insulin Dose at Week 26

End point description:

Average daily bolus Insulin Dose at Week 26 was reported.

APD: All participants who received at least one dose of the study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	285		
Units: Units per day of bolus insulin				
least squares mean (standard error)	27.01 (± 1.182)	34.56 (± 1.156)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 11

Statistical analysis description:

LS Mean was determined by MMRM model using BASELINE + Hemoglobin A1c Stratum at Baseline + Country + Personal Use CGM or FGM at Randomization + Treatment + Time + Treatment*Time (Type III sum of squares) as variables. Variance-covariance structure was set as compound symmetry.

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

Number of subjects included in analysis	560
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-7.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.79
upper limit	-4.3

Secondary: Total Insulin Dose at Week 26

End point title	Total Insulin Dose at Week 26

End point description:

Average total weekly insulin dose at Week 26 was reported.

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	285		
Units: Units per week of insulin				
least squares mean (standard error)	592.92 (± 12.560)	666.43 (± 12.144)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 12

Statistical analysis description:

LS Mean was determined by MMRM model using BASELINE + Hemoglobin A1c Stratum at Baseline + Country + Personal Use CGM or FGM at Randomization + Treatment + Time + Treatment*Time (Type III sum of squares) as variables. Variance-covariance structure was set as compound symmetry.

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

Number of subjects included in analysis	559
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-73.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-107.81
upper limit	-39.2

Secondary: Basal Insulin Dose to Total Insulin Dose Ratio at Week 26

End point title	Basal Insulin Dose to Total Insulin Dose Ratio at Week 26

End point description:

Basal insulin dose to total insulin dose ratio at Week 26 was reported.

APD: All participants who received at least one dose of the study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	285		
Units: Ratio				
least squares mean (standard error)	70.09 (± 0.749)	66.55 (± 0.722)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 13

Statistical analysis description:

LS Mean was determined by MMRM model using BASELINE + Hemoglobin A1c Stratum at Baseline + Country + Personal Use CGM or FGM at Randomization + Treatment + Time + Treatment*Time (Type III sum of squares) as variables. Variance-covariance structure was set as compound symmetry.

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

Number of subjects included in analysis	559
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	3.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.49
upper limit	5.58

Secondary: Hypoglycemia Event Rate

End point title	Hypoglycemia Event Rate

End point description:

Hypoglycemia event rate was reported. 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.

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Baseline to Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	365	365		
Units: Events per year				
arithmetic mean (standard error)	6.58 (± 0.709)	5.94 (± 0.618)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 14

Statistical analysis description:

Group mean was reported and determined by Negative binomial method using Baseline hypoglycemia rate + Hemoglobin A1c at Baseline (%) + Treatment, with log (exposure in days/365.25) as variables.

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

Number of subjects included in analysis	730
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.442
Method	Negative Binomial Model
Parameter estimate	Mean difference (net)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.44

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.

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	365	365		
Units: kilograms (kg)				
least squares mean (standard error)	2.67 (± 0.165)	2.53 (± 0.165)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 15

Statistical analysis description:

LS Mean was determined by MMRM model using BASELINE + Treatment + Time + Treatment*Time (Type III sum of squares) as variables.

Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Glargine
Number of subjects included in analysis	730
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.543
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.14

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.6

Secondary: Treatment Experience for Diabetes Injection Device at Week 26 – Experience Questionnaire (DID-EQ)

End point title	Treatment Experience for Diabetes Injection Device at Week 26 – Experience Questionnaire (DID-EQ)

End point description:

The DID-EQ is a self-administered, 10-item questionnaire designed to assess participants' perceptions of diabetes injection delivery systems for diabetes. The Device Characteristic Subscale is comprised of items 1 to 7 which focus on specific characteristics of injection devices. Each item is rated on a four-point Likert scale. Scores are transformed and range from 0 to 100. Higher scores indicate more positive perceptions of injection device characteristics

APD: All participants who received at least one dose of study drug and had evaluable data for this outcome.

End point type	Secondary

End point timeframe:

Week 26

End point values	500 U/mL - Insulin Efsitora	100 U/mL - Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	286		
Units: Score on a scale				
least squares mean (standard error)	88.1 (± 0.77)	86.3 (± 0.75)		

Statistical analyses

Statistical analysis title	Outcome Measure No. 16

Statistical analysis description:

LS Mean was determined by ANCOVA model using Country + Personal Use CGM or FGM at Randomization + Hemoglobin A1c Stratum at Baseline + Treatment (Type III sum of squares) as variables.

Comparison groups	500 U/mL - Insulin Efsitora v 100 U/mL - Insulin Glargine
Number of subjects included in analysis	560
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.099
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	4

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline Through Safety Follow-Up (Up To 31 Weeks)

Adverse event reporting additional description:

All participants who received at least one dose of the study drug. Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly. Based on the planned safety analysis, adverse event analysis was planned as per the cohorts corresponding to the actual regimen received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	100 U/mL - Insulin Glargine

Reporting group description:

Participants received 100 U/mL insulin glargine administered SC QD along with 100 U/mL insulin lispro given SC.

Reporting group title	500 U/mL - Insulin Efsitora

Reporting group description:

Participants received 500 U/mL insulin efsitora administered SC QW along with 100 U/mL insulin lispro given SC.

Serious adverse events	100 U/mL - Insulin Glargine	500 U/mL - Insulin Efsitora	
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 365 (6.58%)	25 / 365 (6.85%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
cervix carcinoma			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed[1]	0 / 176 (0.00%)	1 / 193 (0.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal cell carcinoma			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lung adenocarcinoma			

alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
aortic stenosis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypotension			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypertensive emergency			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
chest pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pyrexia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
drug hypersensitivity			

alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
acute respiratory failure			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dyspnoea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumothorax			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory distress			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
acute psychosis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bipolar disorder			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
lower limb fracture			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (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 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
arteriosclerosis coronary artery			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
angina pectoris			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac arrest			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	2 / 365 (0.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
acute myocardial infarction			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 365 (0.27%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrioventricular block			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac failure congestive			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
left ventricular failure			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (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 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
cerebrovascular accident			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
migraine			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (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			
deafness neurosensory			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (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 hernia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ascites			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
abdominal pain			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemoperitoneum			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
intestinal obstruction			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (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 26.1			
subjects affected / exposed	1 / 365 (0.27%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
nausea			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
vomiting			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
cholelithiasis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hepatic cirrhosis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 26.1			

subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
postrenal failure			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
nephrolithiasis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract obstruction			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
spinal instability			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (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 26.1			

subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastroenteritis bacterial			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastroenteritis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diabetic foot infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	1 / 365 (0.27%)	3 / 365 (0.82%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
osteomyelitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
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 26.1			
subjects affected / exposed	1 / 365 (0.27%)	0 / 365 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

soft tissue infection			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	0 / 365 (0.00%)	1 / 365 (0.27%)	
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 26.1			
subjects affected / exposed	5 / 365 (1.37%)	5 / 365 (1.37%)	
occurrences causally related to treatment / all	1 / 5	1 / 5	
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.

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

Non-serious adverse events	100 U/mL - Insulin Glargine	500 U/mL - Insulin Efsitora	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 365 (10.96%)	35 / 365 (9.59%)	
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	21 / 365 (5.75%)	23 / 365 (6.30%)	
occurrences (all)	23	25	
influenza			
alternative dictionary used: MedDRA 26.1			
subjects affected / exposed	19 / 365 (5.21%)	14 / 365 (3.84%)	
occurrences (all)	20	17	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 May 2022	- Clarified terms and statements in the Objectives, Endpoints, and Estimands section; - Modified some inclusion and exclusion criteria for more clarity and to address regulator feedback.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported