Clinical trial results:
Protocol I8B-MC-ITRN
A Prospective, Randomized, Double-Blind Comparison of LY900014 to Insulin Lispro, Both in Combination with Insulin Glargine or Insulin Degludec in Adults with Type 2 Diabetes

Summary

EudraCT number	2015-005357-12
Trial protocol	HU ES SK DE IT
Global end of trial date	13 March 2019
Results information	
Result version number	v1 (current)
This version publication date	29 March 2020
First version publication date	29 March 2020

Trial information

Trial identification	
Sponsor protocol code	I8B-MC-ITRN
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03214380
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16314

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	13 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to compare LY900014 to insulin lispro, both in combination with insulin glargine or insulin degludec, in participants with type 2 diabetes (T2D).

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:

Participants were required to use the same basal insulin regimen throughout the study with allowed regimens as follows: 100 U/mL (U-100) basal insulin glargine given SC once or twice daily or U-100 or 200 U/mL (U-200) insulin degludec given SC once daily. Participants may have continued the use of metformin and/or a sodium glucose cotransporter 2 inhibitor (SGLT-2) during the lead-in and treatment phase.

Evidence for comparator: -

Actual start date of recruitment	14 July 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 56
Country: Number of subjects enrolled	Puerto Rico: 14
Country: Number of subjects enrolled	Hungary: 28
Country: Number of subjects enrolled	United States: 187
Country: Number of subjects enrolled	Japan: 93
Country: Number of subjects enrolled	India: 100
Country: Number of subjects enrolled	Russian Federation: 50
Country: Number of subjects enrolled	Spain: 30
Country: Number of subjects enrolled	Korea, Republic of: 69
Country: Number of subjects enrolled	Taiwan: 33
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Mexico: 45
Country: Number of subjects enrolled	Slovakia: 28
Country: Number of subjects enrolled	Australia: 15
Country: Number of subjects enrolled	Germany: 40
Country: Number of subjects enrolled	Czech Republic: 40

Worldwide total number of subjects	837
EEA total number of subjects	175

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)	530
From 65 to 84 years	306
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Maximum Extended Enrollment (MEE) cohorts are implemented in certain countries to meet regulatory requirements for submission. Data from MEE cohort will not be incorporated into the analysis of the global study cohort.

Pre-assignment

Screening details:

The purpose of the Lead-in Period was to titrate basal insulin prior to randomization. Participants were then randomized to receive Insulin lispro (Humalog) or LY900014 in the Treatment Period (Period 2).

Period 1

Period 1 title	Lead-in
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Insulin Lispro (Humalog) Lead-In

Arm description:

100 U/mL Insulin lispro(Humalog) given SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.

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

Dosage and administration details:

100 U/mL Insulin lispro given SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily. Prandial insulin doses were individualized and titrated according to protocol-defined targets.

Arm title	Insulin Lispro (Humalog) Lead-In Maximum Extended Enrollment

Arm description:

100 U/mL Insulin lispro (Humalog) SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.

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

Dosage and administration details:

100 U/mL Insulin lispro given SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily. Prandial insulin doses were individualized and titrated according to protocol-defined targets.

Number of subjects in period 1	Insulin Lispro (Humalog) Lead-In	Insulin Lispro (Humalog) Lead-In Maximum Extended Enrollment
Started	750	183
Received at least 1 dose Lead-in Insulin	750	183
Completed	673	164
Not completed	77	19
Physician decision	6	-
Consent withdrawn by subject	41	14
Adverse event, non-fatal	3	1
Non compliance	1	-
Eligibility criteria	3	-
Natural disaster	9	-
Participant schedule	2	-
Lost to follow-up	4	1
Family emergency	1	-
Protocol deviation	7	3

Period 2	
Period 2 title	Treatment Period
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Insulin Lispro (Humalog)

Arm description:

100 U/mL Insulin lispro given SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.

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

Dosage and administration details:

100 U/mL Insulin lispro given SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily. Prandial insulin doses were individualized and titrated according to protocol-defined targets.

Arm title	LY900014

Arm description:

100 U/mL LY900014 SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.

Arm type	Experimental
Investigational medicinal product name	LY900014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

LY900014 given subcutaneously (SC) with each meal with either 100 U/mL (U-100) basal insulin glargine given SC once or twice daily or U-100 or 200 U/mL (U-200) insulin degludec given SC once daily. Prandial insulin doses were individualized and titrated according to protocol-defined targets.

Arm title	Insulin Lispro (Humalog) Maximum Extended Enrollment (MEE)

Arm description:

100 U/mL Insulin lispro (Humalog) SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.

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

Dosage and administration details:

100 U/mL Insulin lispro given SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily. Prandial insulin doses were individualized and titrated according to protocol-defined targets.

Arm title	LY900014 (MEE)

Arm description:

100 U/mL LY900014 SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.

Arm type	Experimental
Investigational medicinal product name	LY900014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

LY900014 given subcutaneously (SC) with each meal with either 100 U/mL (U-100) basal insulin glargine given SC once or twice daily or U-100 or 200 U/mL (U-200) insulin degludec given SC once daily. Prandial insulin doses were individualized and titrated according to protocol-defined targets.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: The Lead-in Period (Period 1) was used to titrate basal insulin, to allow the participants to reach the target fasting blood glucose (FBG) by the end of this period, prior to randomization. Baseline analysis population is based on all randomized participants. Participants were randomized to Insulin Lispro or LY900014 in Period 2.

Number of subjects in period 2	Insulin Lispro (Humalog)	LY900014	Insulin Lispro (Humalog) Maximum Extended Enrollment (MEE)
Started	337	336	82
Received at least 1 dose of study drug	337	336	82

Completed	319	320	73
Not completed	18	16	9
Consent withdrawn by subject	10	8	7
Non-Compliance with Study Drug	-	-	1
Adverse event, non-fatal	1	1	1
Death	1	2	-
Participant schedule	-	1	-
Treatment interruption	-	1	-
Lost to follow-up	6	3	-

Number of subjects in period 2	LY900014 (MEE)
Started	82
Received at least 1 dose of study drug	82
Completed	71
Not completed	11
Consent withdrawn by subject	11
Non-Compliance with Study Drug	-
Adverse event, non-fatal	-
Death	-
Participant schedule	-
Treatment interruption	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Insulin Lispro (Humalog)
Reporting group description:	
100 U/mL Insulin lispro given SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Reporting group title	LY900014
Reporting group description:	
100 U/mL LY900014 SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Reporting group title	Insulin Lispro (Humalog) Maximum Extended Enrollment (MEE)
Reporting group description:	
100 U/mL Insulin lispro (Humalog) SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Reporting group title	LY900014 (MEE)
Reporting group description:	
100 U/mL LY900014 SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	

Reporting group values	Insulin Lispro (Humalog)	LY900014	Insulin Lispro (Humalog) Maximum Extended Enrollment (MEE)
Number of subjects	337	336	82
Age categorical			
Units: Subjects			
Age continuous			
All randomized participants.			
Units: years			
arithmetic mean	61.0	60.2	56.6
standard deviation	± 9.2	± 9.4	± 9.4
Gender categorical			
All randomized participants.			
Units: Subjects			
Female	162	152	47
Male	175	184	35
Race (NIH/OMB)			
All randomized participants.			
Units: Subjects			
American Indian or Alaska Native	3	1	0
Asian	81	83	70
Native Hawaiian or Other Pacific Islander	1	0	0
Black or African American	16	14	0
White	229	233	12
More than one race	6	5	0
Unknown or Not Reported	1	0	0
Region of Enrollment			
All randomized participants.			

Units: Subjects			
Argentina	29	27	0
Puerto Rico	7	7	0
Hungary	13	15	0
United States	95	92	0
Czechia	20	20	0
Japan	46	47	0
India	9	7	40
Russia	14	13	11
Spain	16	14	0
South Korea	16	16	21
Taiwan	7	8	9
Italy	4	5	0
Mexico	21	22	1
Slovakia	14	14	0
Australia	7	8	0
Germany	19	21	0
Hemoglobin A1c			
All randomized participants.			
Units: percentage of HbA1c			
arithmetic mean	7.31	7.27	7.53
standard deviation	± 0.72	± 0.68	± 0.69

Reporting group values	LY900014 (MEE)	Total	
Number of subjects	82	837	
Age categorical			
Units: Subjects			
Age continuous			
All randomized participants.			
Units: years			
arithmetic mean	57.2		
standard deviation	± 10.1	-	
Gender categorical			
All randomized participants.			
Units: Subjects			
Female	27	388	
Male	55	449	
Race (NIH/OMB)			
All randomized participants.			
Units: Subjects			
American Indian or Alaska Native	0	4	
Asian	69	303	
Native Hawaiian or Other Pacific Islander	0	1	
Black or African American	0	30	
White	13	487	
More than one race	0	11	
Unknown or Not Reported	0	1	
Region of Enrollment			
All randomized participants.			
Units: Subjects			

Argentina	0	56	
Puerto Rico	0	14	
Hungary	0	28	
United States	0	187	
Czechia	0	40	
Japan	0	93	
India	44	100	
Russia	12	50	
Spain	0	30	
South Korea	16	69	
Taiwan	9	33	
Italy	0	9	
Mexico	1	45	
Slovakia	0	28	
Australia	0	15	
Germany	0	40	
Hemoglobin A1c			
All randomized participants.			
Units: percentage of HbA1c			
arithmetic mean	7.67		
standard deviation	± 0.89	-	

End points

End points reporting groups

Reporting group title	Insulin Lispro (Humalog) Lead-In
Reporting group description:	
100 U/mL Insulin lispro(Humalog) given SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Reporting group title	Insulin Lispro (Humalog) Lead-In Maximum Extended Enrollment
Reporting group description:	
100 U/mL Insulin lispro (Humalog) SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Reporting group title	Insulin Lispro (Humalog)
Reporting group description:	
100 U/mL Insulin lispro given SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Reporting group title	LY900014
Reporting group description:	
100 U/mL LY900014 SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Reporting group title	Insulin Lispro (Humalog) Maximum Extended Enrollment (MEE)
Reporting group description:	
100 U/mL Insulin lispro (Humalog) SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Reporting group title	LY900014 (MEE)
Reporting group description:	
100 U/mL LY900014 SC with each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Subject analysis set title	Insulin Lispro (Humalog)
Subject analysis set type	Per protocol
Subject analysis set description:	
Insulin lispro given SC with each meal with either U-100 basal insulin glargine given SC once or twice daily or U-100 or U-200 insulin degludec given SC once daily.	
Subject analysis set title	LY900014
Subject analysis set type	Per protocol
Subject analysis set description:	
LY900014 given subcutaneously (SC) with each meal with either 100 U/mL (U-100) basal insulin glargine given SC once or twice daily or U-100 or 200 U/mL (U-200) insulin degludec given SC once daily.	

Primary: Change from Baseline in Hemoglobin A1c (HbA1c) Efficacy Estimand at Week 26

End point title	Change from Baseline in Hemoglobin A1c (HbA1c) Efficacy Estimand at Week 26
End point description:	
Change from baseline in HbA1c was performed using mixed model repeated measure (MMRM) including fixed class effects of treatment, strata (pooled country, type of basal insulin, and number of prandial doses at study entry), visit, and treatment-by-visit interaction, as well as the continuous, fixed covariates of baseline value. The efficacy estimand included participant data when baseline and at least one post-baseline measurement were available prior to permanent discontinuation of study drug. Analysis Population Description (APD): All randomized participants with baseline and at least one post-baseline HbA1c data. As pre-specified in the analysis plan, outcome measures will not be reported for the Maximum Extended Enrollment (MEE) arms/groups but only for the main global study arms/groups.	
End point type	Primary

End point timeframe:

Baseline, Week 26

End point values	Insulin Lispro (Humalog)	LY900014		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	335	334		
Units: percentage of HbA1c				
least squares mean (standard error)	-0.43 (± 0.042)	-0.38 (± 0.042)		

Statistical analyses

Statistical analysis title	Change from Baseline in Hemoglobin A1c (HbA1c)
Comparison groups	Insulin Lispro (Humalog) v LY900014
Number of subjects included in analysis	669
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Least Square Mean Difference (LSMean)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.16

Secondary: 1-hour Postprandial Glucose (PPG) Excursion during Mixed-Meal Tolerance Test (MMTT) Efficacy Estimand

End point title	1-hour Postprandial Glucose (PPG) Excursion during Mixed-Meal Tolerance Test (MMTT) Efficacy Estimand

End point description:

1-hour PPG excursion during MMTT uses the analysis of covariance (ANCOVA) model with strata (pooled country, type of basal insulin, number of prandial doses at study entry, and HbA1c stratum) and treatment as fixed effects and baseline as a covariate. The efficacy estimand included participant data when baseline and at least one post-baseline measurement were available prior to permanent discontinuation of study drug.

APD: All randomized participants with baseline and at least one post-baseline 1-hour PPG excursion data. As pre-specified in the analysis plan, outcome measures will not be reported for the MEE arms/groups but only for the main global study arms/groups.

End point type	Secondary

End point timeframe:

Week 26

End point values	Insulin Lispro (Humalog)	LY900014		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	307	304		
Units: milligrams per deciliter (mg/dL)				
least squares mean (standard error)	74.9 (± 3.60)	63.1 (± 3.60)		

Statistical analyses

Statistical analysis title	1-hour Postprandial Glucose (PPG) Excursion
Comparison groups	Insulin Lispro (Humalog) v LY900014
Number of subjects included in analysis	611
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-11.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.1
upper limit	-5.5

Secondary: 2-hour PPG Excursion during MMTT Efficacy Estimand

End point title	2-hour PPG Excursion during MMTT Efficacy Estimand

End point description:

2-hour PPG excursion during MMTT uses the ANCOVA model with strata (pooled country, type of basal insulin, number of prandial doses at study entry, and HbA1c stratum) and treatment as fixed effects and baseline as a covariate. The efficacy estimand included participant data when baseline and at least one post-baseline measurement were available prior to permanent discontinuation of study drug.

APD: All randomized participants with baseline and at least one post-baseline 2-hour PPG excursion data. As pre-specified in the analysis plan, outcome measures will not be reported for the MEE arms/groups but only for the main global study arms/groups.

End point type	Secondary

End point timeframe:

Week 26

End point values	Insulin Lispro (Humalog)	LY900014		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	306	305		
Units: mg/dL				
least squares mean (standard error)	97.8 (± 4.50)	80.4 (± 4.50)		

Statistical analyses

Statistical analysis title	2-hour PPG Excursion during MMTT Efficacy Estimand
Comparison groups	Insulin Lispro (Humalog) v LY900014
Number of subjects included in analysis	611
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-17.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.3
upper limit	-9.5

Secondary: Rate of Severe Hypoglycemia

End point title	Rate of Severe Hypoglycemia

End point description:

Rate of severe hypoglycemia events per 100 years during a defined period was calculated by total number of severe hypoglycemia episodes within the period divided by the cumulative days on treatment from all participants within a treatment group *36525. Severe hypoglycemia is defined as an event requiring assistance of another person to administer carbohydrate, glucagon, or other resuscitative actions. During these episodes, the participant has an altered mental status and cannot assist in his or her own care, or may be semiconscious or unconscious, or experience com with or without seizures, and may require parenteral therapy.

APD: All randomized participants with evaluable hypoglycemic data. As pre-specified in the analysis plan, outcome measures will not be reported for the MEE arms/groups but only for the main global study arms/groups.

End point type	Secondary

End point timeframe:

Baseline through Week 26

End point values	Insulin Lispro (Humalog)	LY900014		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	337	336		
Units: Events per 100 participant years				
number (not applicable)	4.19	2.44		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Documented Symptomatic Hypoglycemia

End point title	Rate of Documented Symptomatic Hypoglycemia

End point description:

Documented symptomatic hypoglycemia is an event during which typical symptoms of hypoglycemia are accompanied by blood glucose (BG) of <54 mg/dL [3.0 millimole per liter (mmol/L)]. The rate of documented symptomatic hypoglycemia was estimated by negative binomial model: number of episodes = treatment with log (treatment exposure in days/365.25) as an offset variable.

APD: All randomized participants with evaluable hypoglycemic data. As pre-specified in the analysis plan, outcome measures will not be reported for the MEE arms/groups but only for the main global study arms/groups.

End point type	Secondary

End point timeframe:

Baseline through Week 26

End point values	Insulin Lispro (Humalog)	LY900014		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	337	336		
Units: Events per participant per year				
least squares mean (standard error)	1.34 (± 0.164)	2.21 (± 0.318)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 1,5-Anhydroglucitol (1,5-AG) at Week 26

End point title	Change From Baseline in 1,5-Anhydroglucitol (1,5-AG) at Week 26

End point description:

Change From baseline in 1,5-AG LSMean was calculated using Mixed Model Repeated Measures (MMRM) model including fixed class effects of treatment, strata (pooled country, type of basal insulin, HbA1c stratum and number of prandial doses at study entry), visit, and treatment-by-visit interaction, as well as the continuous, fixed covariates of baseline value. The analysis included data collected prior to permanent discontinuation of study drug.

APD: All randomized participants with baseline and at least one post-baseline 1,5-AG data. As pre-specified in the analysis plan, outcome measures will not be reported for the MEE arms/groups but only for the main global study arms/groups.

End point type	Secondary

End point timeframe:
Baseline, Week 26

End point values	Insulin Lispro (Humalog)	LY900014		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	334	331		
Units: milligram per liter (mg/L)				
least squares mean (standard error)	2.15 (± 0.234)	1.99 (± 0.235)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in 10-Point Self-Monitoring Blood Glucose (SMBG) Values at Week 26

End point title	Change from Baseline in 10-Point Self-Monitoring Blood Glucose (SMBG) Values at Week 26

End point description:

Change from baseline in 10-point SMBG values was calculated using MMRM model including fixed class effects of treatment, strata (pooled country, type of basal insulin, and number of prandial doses at study entry), visit, and treatment-by-visit interaction, as well as the continuous, fixed covariates of baseline value. The efficacy estimand included participant data when baseline and at least one post-baseline measurement prior to permanent discontinuation of study drug.

APD: All randomized participants with baseline and at least one post-baseline SMBG data. As pre-specified in the analysis plan, outcome measures will not be reported for the MEE arms/groups but only for the main global study arms/groups.

End point type	Secondary

End point timeframe:
Baseline, Week 26

End point values	Insulin Lispro (Humalog)	LY900014		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	276	270		
Units: mg/dL				
least squares mean (standard error)				
Morning Premeal	-0.8 (± 2.72)	1.5 (± 2.74)		
Morning 1-hour Postmeal	-2.0 (± 3.44)	-14.1 (± 3.44)		
Morning 2-hour Postmeal	0.6 (± 3.38)	-14.9 (± 3.38)		
Midday Premeal	2.4 (± 2.83)	4.1 (± 2.84)		
Midday 1-hour Postmeal	3.0 (± 3.48)	-2.0 (± 3.47)		
Midday 2-hour Postmeal	-2.2 (± 3.28)	-6.5 (± 3.27)		
Evening Premeal	7.0 (± 3.38)	10.1 (± 3.38)		
Evening 1-hour Postmeal	-2.1 (± 3.24)	-3.0 (± 3.27)		

Evening 2-hour Postmeal	0.2 (± 3.68)	-2.1 (± 3.73)		
Bedtime	-3.4 (± 4.00)	-2.2 (± 4.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Insulin Dose at Week 26

End point title	Change from Baseline in Insulin Dose at Week 26

End point description:

Change from baseline in insulin dose was analyzed using mixed model repeated measure (MMRM) including fixed class effects of treatment, strata (pooled country, type of basal insulin, HbA1c stratum and number of prandial doses at study entry), visit, and treatment-by-visit interaction, as well as the continuous, fixed covariates of baseline value. The analysis included data prior to permanent discontinuation (d/c) of study drug (IP).

APD: All randomized participants with baseline and at least one post-baseline basal insulin dose data. As pre-specified in the analysis plan, outcome measures will not be reported for the MEE arms/groups but only for the main global study arms/groups.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Insulin Lispro (Humalog)	LY900014		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	330	330		
Units: Units (U)				
least squares mean (standard error)				
Basal Insulin Dose (n=317, 323)	4.2 (± 0.82)	4.6 (± 0.81)		
Prandial Insulin Dose (n=330, 330)	8.3 (± 1.41)	12.0 (± 1.41)		
Total Daily Insulin Dose (n=316, 321)	12.1 (± 1.93)	17.3 (± 1.92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Insulin Treatment Satisfaction Questionnaire (ITSQ) Regimen Inconvenience Domain Score at Week 26

End point title	Change from Baseline in Insulin Treatment Satisfaction Questionnaire (ITSQ) Regimen Inconvenience Domain Score at Week 26

End point description:

ITSQ is a validated instrument containing 22 items that assess treatment satisfaction for participants with diabetes and on insulin. The questionnaire measures satisfaction from the following 5 domains: Inconvenience of Regimen, Lifestyle Flexibility, Glycemic Control, Hypoglycemic Control, and Insulin Delivery Device. Data presented are the transformed overall score on a scale of 0-100, where higher

scores indicate better treatment satisfaction. Change from baseline in ITSQ regimen inconvenience domain score was calculated using the ANCOVA model with strata (pooled country, type of basal insulin, number of prandial doses at study entry, and HbA1c stratum), and treatment as fixed effects and baseline as covariate. Analysis includes data collected prior to d/c of IP.

APD: All randomized participants with baseline and post-baseline data. As pre-specified in the analysis plan, outcome measures will not be reported for the MEE arms/groups but only for the main global study arms/groups.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Insulin Lispro (Humalog)	LY900014		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	319[1]	319[2]		
Units: units on a scale				
least squares mean (standard error)	-0.9 (± 1.36)	-2.4 (± 1.37)		

Notes:

[1] - Missing endpoints were imputed by applying the LOCF method to post-baseline data.

[2] - Missing endpoints were imputed by applying the LOCF method to post-baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in ITSQ Lifestyle Flexibility Domain Score at Week 26

End point title	Change from Baseline in ITSQ Lifestyle Flexibility Domain Score at Week 26

End point description:

ITSQ is a validated instrument containing 22 items that assess treatment satisfaction for participants with diabetes and on insulin. The questionnaire measures satisfaction from the following 5 domains: Inconvenience of Regimen, Lifestyle Flexibility, Glycemic Control, Hypoglycemic Control, and Insulin Delivery Device. Data presented are the transformed overall score on a scale of 0-100, where higher scores indicate better treatment satisfaction. Change from baseline in ITSQ lifestyle flexibility domain score was calculated using the ANCOVA model with strata (pooled country, type of basal insulin, number of prandial doses at study entry, and HbA1c stratum), and treatment as fixed effects and baseline as covariate. Analysis includes data collected prior to d/c of IP.

APD: All randomized participants with baseline and post-baseline data. As pre-specified in the analysis plan, outcome measures will not be reported for the MEE arms/groups but only for the main global study arms/groups.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Insulin Lispro (Humalog)	LY900014		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	319[3]	319[4]		
Units: units on a scale				
least squares mean (standard error)	1.4 (± 1.60)	0.2 (± 1.60)		

Notes:

[3] - Missing endpoints were imputed by applying the LOCF method to the post-baseline data.

[4] - Missing endpoints were imputed by applying the LOCF method to the post-baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with HbA1c <7%

End point title	Number of Participants with HbA1c <7%

End point description:

Number of participants with HbA1c <7% at Week 26.

APD: All participants with baseline and 1 post-baseline observation while on study drug. As pre-specified in the analysis plan, outcome measures will not be reported for the MEE arms/groups but only for the main global study arms/groups.

End point type	Secondary

End point timeframe:

Week 26

End point values	Insulin Lispro (Humalog)	LY900014		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	320	316		
Units: Count of participants				
number (not applicable)	168	184		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to 30 weeks	
Adverse event reporting additional description:	
I8B-MC-ITRN	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	Insulin Lispro (Humalog) Lead-in
Reporting group description: -	
Reporting group title	Insulin Lispro (Humalog)
Reporting group description: -	
Reporting group title	LY900014
Reporting group description: -	
Reporting group title	Insulin Lispro (Humalog) Lead-in Maximum Extended Enrollment
Reporting group description: -	
Reporting group title	Insulin Lispro (Humalog) Maximum Extended Enrollment
Reporting group description: -	
Reporting group title	LY900014 Maximum Extended Enrollment Cohort
Reporting group description: -	

Serious adverse events	Insulin Lispro (Humalog) Lead-in	Insulin Lispro (Humalog)	LY900014
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 750 (1.73%)	26 / 337 (7.72%)	26 / 336 (7.74%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
clear cell renal cell carcinoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
meningioma			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal neoplasm			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intermittent claudication			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 750 (0.13%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral arterial occlusive disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral artery stenosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral vascular disorder			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General disorders and administration site conditions			
non-cardiac chest pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sudden death			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Immune system disorders			
drug hypersensitivity			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 750 (0.13%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
acute pulmonary oedema			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
acute respiratory failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	2 / 336 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
bronchitis chronic			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	3 / 336 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dyspnoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	2 / 336 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
laryngeal disorder			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 750 (0.13%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
blood potassium decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
concussion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 750 (0.13%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fall			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 750 (0.13%)	1 / 337 (0.30%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
heat stroke			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ligament sprain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
multiple fractures			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spinal compression fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
angina pectoris			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
angina unstable			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrial fibrillation			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
coronary artery stenosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	2 / 337 (0.59%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myocardial infarction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 750 (0.13%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
carpal tunnel syndrome			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoglycaemic coma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 750 (0.13%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lumbar radiculopathy			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
syncope			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transient ischaemic attack			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
cataract			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 750 (0.13%)	1 / 337 (0.30%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
eye haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
papilloedema			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 750 (0.13%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
gastritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
bile duct stone			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 750 (0.13%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholelithiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
diabetic ulcer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
nephrolithiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ureteric compression			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intervertebral disc protrusion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lumbar spinal stenosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteoarthritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
empyema			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
eye infection viral			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastroenteritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteomyelitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 750 (0.13%)	0 / 337 (0.00%)	4 / 336 (1.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
pyelonephritis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
septic shock			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
sinusitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

urinary tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 750 (0.13%)	0 / 337 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
hypoglycaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 750 (0.27%)	5 / 337 (1.48%)	3 / 336 (0.89%)
occurrences causally related to treatment / all	2 / 2	4 / 6	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
shock hypoglycaemic			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 750 (0.00%)	1 / 337 (0.30%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Insulin Lispro (Humalog) Lead-in Maximum Extended Enrollment	Insulin Lispro (Humalog) Maximum Extended Enrollment	LY900014 Maximum Extended Enrollment Cohort
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 183 (1.64%)	4 / 82 (4.88%)	2 / 82 (2.44%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
clear cell renal cell carcinoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
meningioma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

renal neoplasm			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intermittent claudication			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral arterial occlusive disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral artery stenosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral vascular disorder			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
non-cardiac chest pain			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sudden death			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
drug hypersensitivity			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
acute pulmonary oedema			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
acute respiratory failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bronchitis chronic			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chronic obstructive pulmonary disease			
alternative dictionary used:			

MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dyspnoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
laryngeal disorder			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
blood potassium decreased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
concussion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fall			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
heat stroke			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ligament sprain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
multiple fractures			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spinal compression fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	1 / 82 (1.22%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
angina pectoris			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
angina unstable			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrial fibrillation			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
coronary artery stenosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myocardial infarction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
carpal tunnel syndrome			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	1 / 82 (1.22%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoglycaemic coma			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lumbar radiculopathy			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	1 / 82 (1.22%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
syncope			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	1 / 82 (1.22%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transient ischaemic attack			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
cataract			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
eye haemorrhage			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
papilloedema			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
gastritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 183 (0.55%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
bile duct stone			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholelithiasis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
diabetic ulcer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 183 (0.55%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nephrolithiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ureteric compression			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intervertebral disc protrusion			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lumbar spinal stenosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteoarthritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
empyema			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 183 (0.55%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
eye infection viral			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastroenteritis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteomyelitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyelonephritis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
septic shock			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sinusitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	1 / 82 (1.22%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
hypoglycaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
shock hypoglycaemic			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 183 (0.00%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Insulin Lispro (Humalog) Lead-in	Insulin Lispro (Humalog)	LY900014
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 750 (5.87%)	60 / 337 (17.80%)	79 / 336 (23.51%)
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	11 / 750 (1.47%)	10 / 337 (2.97%)	11 / 336 (3.27%)
occurrences (all)	11	10	12
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	23 / 750 (3.07%)	38 / 337 (11.28%)	47 / 336 (13.99%)
occurrences (all)	25	47	56
upper respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	13 / 750 (1.73%)	20 / 337 (5.93%)	27 / 336 (8.04%)
occurrences (all)	13	21	29

Non-serious adverse events	Insulin Lispro (Humalog) Lead-in Maximum Extended Enrollment	Insulin Lispro (Humalog) Maximum Extended Enrollment	LY900014 Maximum Extended Enrollment Cohort
Total subjects affected by non-serious adverse events			

subjects affected / exposed	12 / 183 (6.56%)	8 / 82 (9.76%)	5 / 82 (6.10%)
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 183 (1.09%)	5 / 82 (6.10%)	0 / 82 (0.00%)
occurrences (all)	2	5	0
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	7 / 183 (3.83%)	4 / 82 (4.88%)	5 / 82 (6.10%)
occurrences (all)	7	4	5
upper respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	3 / 183 (1.64%)	0 / 82 (0.00%)	0 / 82 (0.00%)
occurrences (all)	3	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 May 2017	- Immunogenicity follow-up shortened. - Primary analysis modified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As pre-specified in the analysis plan, outcome measures will not be reported for the Maximum Extended Enrollment (MEE) arms/groups but only for the main global study arms/groups.

Notes: