Clinical trial results:
A Prospective, Randomized, Double-Blind Comparison of LY900014 to Insulin Lispro with an Open-Label Postprandial LY900014 Treatment Group, in Combination with Insulin Glargine or Insulin Degludec, in Adults with Type 1 Diabetes

Summary

EudraCT number	2015-005356-99
Trial protocol	SE ES SK DE AT PL GR IT RO
Global end of trial date	22 August 2019

Results information

Result version number	v1 (current)
This version publication date	03 May 2020
First version publication date	03 May 2020

Trial information

Trial identification

Sponsor protocol code	I8B-MC-ITRM

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03214367
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16313

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 August 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the efficacy of the study drug LY900014 compared to insulin lispro, both in combination with insulin glargine or insulin degludec, in adults with type 1 diabetes (T1D).

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	17 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: 42
Country: Number of subjects enrolled	Puerto Rico: 14
Country: Number of subjects enrolled	Romania: 92
Country: Number of subjects enrolled	United States: 399
Country: Number of subjects enrolled	Japan: 168
Country: Number of subjects enrolled	India: 55
Country: Number of subjects enrolled	Russian Federation: 33
Country: Number of subjects enrolled	Spain: 78
Country: Number of subjects enrolled	Greece: 77
Country: Number of subjects enrolled	New Zealand: 24
Country: Number of subjects enrolled	Austria: 27
Country: Number of subjects enrolled	Sweden: 13
Country: Number of subjects enrolled	Taiwan: 46
Country: Number of subjects enrolled	Poland: 128
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	Mexico: 49
Country: Number of subjects enrolled	Slovakia: 16
Country: Number of subjects enrolled	Australia: 30
Country: Number of subjects enrolled	Germany: 78

Worldwide total number of subjects	1392
EEA total number of subjects	532

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)	1276
From 65 to 84 years	116
85 years and over	0

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 study consists of 2 double-blind arms (LY900014 and Insulin Lispro (Humalog)) and one Open-label treatment group (LY900014 Postmeal).
Double-blind group: The study included 8-week lead-in period followed by a 52-week treatment period.
Open-label treatment group: The treatment period ended after 26 weeks.

Period 1

Period 1 title	Lead-in Period
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 given subcutaneously (SC) 0-2 minutes before 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	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 subcutaneously (SC) 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily. Preprandial insulin doses were individualized and titrated according to protocol-defined targets.

Arm title	Insulin Lispro (Humalog) Lead-in-MEE

Arm description:

100 U/mL Insulin lispro given subcutaneously (SC) 0-2 minutes before 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	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 subcutaneously (SC) 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily. Preprandial 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-MEE
Started	1316	76
Completed	1222	74
Not completed	94	2
Consent withdrawn by subject	50	2
Physician decision	12	-
not captured	1	-
Adverse event, non-fatal	3	-
Sponsor Decision	11	-
Lost to follow-up	12	-
Protocol deviation	5	-

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 subcutaneously (SC) 0-2 minutes before 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	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 subcutaneously (SC) 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily. Preprandial insulin doses were individualized and titrated according to protocol-defined targets.

Arm title	LY900014

Arm description:

100 U/mL LY900014 given SC 0-2 minutes before 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	Ultra-Rapid Lispro
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL LY900014 given SC 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily. Preprandial insulin doses were individualized and titrated according to protocol-defined targets.

Arm title	LY900014 Postmeal

Arm description:

100 U/mL LY900014 given SC 20 minutes after the start of 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	Ultra-Rapid Lispro
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL LY900014 given SC 20 minutes after the start of 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)-MEE

Arm description:

100 U/mL Insulin lispro given subcutaneously (SC) 0-2 minutes before 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	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 subcutaneously (SC) 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily. Preprandial insulin doses were individualized and titrated according to protocol-defined targets.

Arm title	LY900014-MEE

Arm description:

100 U/mL LY900014 given SC 0-2 minutes before 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	Ultra-Rapid Lispro
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL LY900014 given SC 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily. Preprandial insulin doses were individualized and titrated according to protocol-defined targets.

Arm title	LY900014 Postmeal-MEE

Arm description:

100 U/mL LY900014 given SC 20 minutes after the start of 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	Ultra-Rapid Lispro
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

100 U/mL LY900014 given SC 20 minutes after the start of 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.

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[2]	Insulin Lispro (Humalog)	LY900014	LY900014 Postmeal
Started	442	451	329
Completed	408	418	310
Not completed	34	33	19
Adverse event, serious fatal	1	1	1
Physician decision	1	2	-
Consent withdrawn by subject	20	23	14
Adverse event, non-fatal	1	4	2
Sponsor Decision	3	-	-
Lost to follow-up	5	3	2
Protocol deviation	3	-	-

Number of subjects in period 2[2]	Insulin Lispro (Humalog)-MEE	LY900014-MEE	LY900014 Postmeal-MEE
Started	31	21	22
Completed	28	19	21
Not completed	3	2	1
Adverse event, serious fatal	-	-	-
Physician decision	-	-	-
Consent withdrawn by subject	1	1	1
Adverse event, non-fatal	-	-	-
Sponsor Decision	-	-	-
Lost to follow-up	2	1	-
Protocol deviation	-	-	-

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The reported number is from Lead-In period.

Baseline characteristics

Reporting groups	
Reporting group title	Insulin Lispro (Humalog)
Reporting group description:	
100 U/mL Insulin lispro given subcutaneously (SC) 0-2 minutes before 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 given SC 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Reporting group title	LY900014 Postmeal
Reporting group description:	
100 U/mL LY900014 given SC 20 minutes after the start of 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)-MEE
Reporting group description:	
100 U/mL Insulin lispro given subcutaneously (SC) 0-2 minutes before 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 given SC 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Reporting group title	LY900014 Postmeal-MEE
Reporting group description:	
100 U/mL LY900014 given SC 20 minutes after the start of 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	LY900014 Postmeal
Number of subjects	442	451	329
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	44.5	44.1	44.5
standard deviation	± 13.6	± 13.7	± 14.3
Gender categorical			
Units: Subjects			
Female	186	201	147
Male	256	250	182
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	33	35	35
Not Hispanic or Latino	397	399	283
Unknown or Not Reported	12	17	11
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	1	2
Asian	78	86	63

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	9	7	5
White	344	346	254
More than one race	11	10	5
Unknown or Not Reported	0	1	0
Region of Enrollment Units: Subjects			
Argentina	11	14	14
Puerto Rico	2	3	2
Romania	34	30	23
United States	129	134	98
Japan	59	62	46
India	10	10	8
Russia	8	11	5
Spain	25	30	20
Greece	26	28	21
New Zealand	10	11	3
Austria	9	6	7
Sweden	5	2	3
Taiwan	9	11	8
Poland	49	47	27
Italy	9	7	4
Mexico	6	4	8
Slovakia	6	6	4
Australia	9	10	7
Germany	26	25	21
Hemoglobin A1c (HbA1c)			
The data presented is following 8 weeks of basal insulin optimization.			
Units: Percentage of HbA1c			
arithmetic mean	7.33	7.34	7.36
standard deviation	± 0.67	± 0.65	± 0.64

Reporting group values	Insulin Lispro (Humalog)-MEE	LY900014-MEE	LY900014 Postmeal-MEE
Number of subjects	31	21	22
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	32.1	32.4	31.5
standard deviation	± 12.3	± 12.4	± 12.7
Gender categorical Units: Subjects			
Female	14	9	13
Male	17	12	9
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	12	8	9
Not Hispanic or Latino	18	12	12
Unknown or Not Reported	1	1	1

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	18	11	10
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	12	9	11
More than one race	0	1	0
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Argentina	0	0	0
Puerto Rico	0	0	0
Romania	0	0	0
United States	0	0	0
Japan	0	0	0
India	10	8	6
Russia	2	1	3
Spain	0	0	0
Greece	0	0	0
New Zealand	0	0	0
Austria	0	0	0
Sweden	0	0	0
Taiwan	8	4	4
Poland	0	0	0
Italy	0	0	0
Mexico	11	8	9
Slovakia	0	0	0
Australia	0	0	0
Germany	0	0	0
Hemoglobin A1c (HbA1c)			
The data presented is following 8 weeks of basal insulin optimization.			
Units: Percentage of HbA1c			
arithmetic mean	7.52	7.28	7.60
standard deviation	± 0.99	± 0.67	± 0.62

Reporting group values	Total		
Number of subjects	1296		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	570		
Male	726		

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	132		
Not Hispanic or Latino	1121		
Unknown or Not Reported	43		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	5		
Asian	266		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	21		
White	976		
More than one race	27		
Unknown or Not Reported	1		
Region of Enrollment Units: Subjects			
Argentina	39		
Puerto Rico	7		
Romania	87		
United States	361		
Japan	167		
India	52		
Russia	30		
Spain	75		
Greece	75		
New Zealand	24		
Austria	22		
Sweden	10		
Taiwan	44		
Poland	123		
Italy	20		
Mexico	46		
Slovakia	16		
Australia	26		
Germany	72		
Hemoglobin A1c (HbA1c)			
The data presented is following 8 weeks of basal insulin optimization.			
Units: Percentage of HbA1c			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Insulin Lispro (Humalog) Lead-in
Reporting group description:	
100 U/mL Insulin lispro given subcutaneously (SC) 0-2 minutes before 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-MEE
Reporting group description:	
100 U/mL Insulin lispro given subcutaneously (SC) 0-2 minutes before 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 subcutaneously (SC) 0-2 minutes before 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 given SC 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Reporting group title	LY900014 Postmeal
Reporting group description:	
100 U/mL LY900014 given SC 20 minutes after the start of 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)-MEE
Reporting group description:	
100 U/mL Insulin lispro given subcutaneously (SC) 0-2 minutes before 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 given SC 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Reporting group title	LY900014 Postmeal-MEE
Reporting group description:	
100 U/mL LY900014 given SC 20 minutes after the start of 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:	
100 U/mL Insulin lispro given subcutaneously (SC) 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Subject analysis set title	LY900014
Subject analysis set type	Per protocol
Subject analysis set description:	
100 U/mL LY900014 given SC 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.	
Subject analysis set title	LY900014 Postmeal
Subject analysis set type	Per protocol
Subject analysis set description:	
100 U/mL LY900014 given SC 20 minutes after the start of 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)-MEE
Subject analysis set type	Per protocol
Subject analysis set description:	
100 U/mL Insulin lispro given subcutaneously (SC) 0-2 minutes before each meal with either basal	

insulin glargine given SC once or twice daily or insulin degludec given SC once daily.

Subject analysis set title	LY900014-MEE
Subject analysis set type	Per protocol

Subject analysis set description:

100 U/mL LY900014 given SC 0-2 minutes before each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.

Subject analysis set title	LY900014 Postmeal-MEE
Subject analysis set type	Per protocol

Subject analysis set description:

100 U/mL LY900014 given SC 20 minutes after the start of each meal with either basal insulin glargine given SC once or twice daily or insulin degludec given SC once daily.

Primary: Change from Baseline in Hemoglobin A1c (HbA1c)

End point title	Change from Baseline in Hemoglobin A1c (HbA1c)[1]

End point description:

HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time.
Least Squares (LS) mean was determined by mixed model repeated measure (MMRM) model with strata (pooled country, type of basal insulin, prandial insulin dosing plan, 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.

Analysis Population Description (APD): All randomized participants with baseline and at least 1 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

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As 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 values	Insulin Lispro (Humalog)	LY900014	LY900014 Postmeal	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	417	428	309	
Units: Percentage of HbA1c				
least squares mean (standard error)	-0.05 (± 0.031)	-0.13 (± 0.031)	0.08 (± 0.035)	

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	845
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.06
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.08

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0

Statistical analysis title	Change from Baseline in Hemoglobin A1c (HbA1c)
Comparison groups	Insulin Lispro (Humalog) v LY900014 Postmeal
Number of subjects included in analysis	726
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.22

Secondary: Change from baseline in 1-hour Postprandial Glucose (PPG) Excursion during Mixed-Meal Tolerance Test (MMTT)

End point title	Change from baseline in 1-hour Postprandial Glucose (PPG) Excursion during Mixed-Meal Tolerance Test (MMTT)[2]

End point description:

A standardized MMTT was used to characterize postprandial glucose control following administration of the study insulin. Serum glucose measured at 1-hour timepoint after the start of meal minus fasting serum glucose. 1-hour PPG excursion during MMTT uses the ANCOVA model with strata (pooled country, type of basal insulin, prandial insulin dosing plan, and HbA1c stratum) and treatment as fixed effects and baseline as a covariate. The efficacy estimand included data collected from all randomized participants prior to permanent discontinuation of study drug.

APD: All randomized participants with baseline and at least 1 post-baseline 1-hour PPG excursion 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	Secondary

End point timeframe:

Baseline, Week 26

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As 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 values	Insulin Lispro (Humalog)	LY900014	LY900014 Postmeal	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	403	278	
Units: milligrams per deciliter (mg/dL)				
least squares mean (standard error)	-0.7 (± 3.34)	-28.6 (± 3.33)	12.5 (± 3.74)	

Statistical analyses

Statistical analysis title	Change From Baseline in 1-hour PPG
Comparison groups	Insulin Lispro (Humalog) v LY900014
Number of subjects included in analysis	793
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-27.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.3
upper limit	-20.6

Statistical analysis title	Change From Baseline in 1-hour PPG
Comparison groups	Insulin Lispro (Humalog) v LY900014 Postmeal
Number of subjects included in analysis	668
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	13.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	21.4

Secondary: Change From Baseline in 2-hour PPG Excursion during MMTT

End point title	Change From Baseline in 2-hour PPG Excursion during MMTT[3]

End point description:

A standardized MMTT was used to characterize postprandial glucose control following administration of the study insulin. Serum glucose measured at 2-hour timepoint after the start of meal minus fasting serum glucose. 2 hour PPG excursion during MMTT uses the ANCOVA model with strata (pooled country,

type of basal insulin, prandial insulin dosing plan, and HbA1c stratum) and treatment as fixed effects and baseline as a covariate. The efficacy estimand included data collected from all randomized participants prior to permanent discontinuation of study drug.

APD: All randomized participants with baseline and 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:

Baseline, Week 26

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As 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 values	Insulin Lispro (Humalog)	LY900014	LY900014 Postmeal	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	401	278	
Units: mg/dL				
least squares mean (standard error)	-3.5 (± 4.51)	-34.7 (± 4.50)	-10.2 (± 5.04)	

Statistical analyses

Statistical analysis title	Change From Baseline in 2-hour PPG
Comparison groups	Insulin Lispro (Humalog) v LY900014
Number of subjects included in analysis	792
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-31.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.1
upper limit	-21.2

Statistical analysis title	Change From Baseline in 2-hour PPG
Comparison groups	Insulin Lispro (Humalog) v LY900014 Postmeal
Number of subjects included in analysis	669
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.235
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-6.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.6
upper limit	4.3

Secondary: Rate of Severe Hypoglycemia

End point title	Rate of Severe Hypoglycemia[4]

End point description:

Hypoglycemic event is defined as an event which is associated with reported signs and symptoms of hypoglycemia, and/or a documented blood glucose (BG) concentration of <=70 milligram per deciliter (mg/dL) (3.9 millimoles per liter [mmol/L]). 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 coma with or without seizures, and may require parenteral therapy. 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 *365.25.

APD: All randomized participants with evaluable hypoglycemic data.

End point type	Secondary

End point timeframe:

Baseline through Week 26

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: 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 values	Insulin Lispro (Humalog)	LY900014	LY900014 Postmeal	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	442	451	329	
Units: Events/Participants/100 Years				
number (not applicable)	18.34	16.50	13.70	

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Documented Symptomatic Hypoglycemia

End point title	Rate of Documented Symptomatic Hypoglycemia[5]

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

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As 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 values	Insulin Lispro (Humalog)	LY900014	LY900014 Postmeal	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	442	451	329	
Units: Events per participant per Year				
least squares mean (standard error)	7.35 (± 0.697)	6.71 (± 0.479)	7.75 (± 0.582)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Change From Baseline in 1,5-Anhydroglucitol (1,5-AG)[6]

End point description:

1,5-anhydroglucitol (1,5-AG) is a marker of short-term glycemic control especially postprandial hyperglycemia. 1,5-AG accurately predicts rapid changes in glycemia and is tightly associated with glucose fluctuations and postprandial glucose. LS Mean was calculated 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.

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

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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 values	Insulin Lispro (Humalog)	LY900014	LY900014 Postmeal	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	417	430	307	
Units: milligram per liter (mg/L)				
least squares mean (standard error)	-0.22 (± 0.109)	0.19 (± 0.108)	-0.38 (± 0.124)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline in 10-Point Self-Monitoring Blood Glucose (SMBG) Values[7]

End point description:

SMBG 10-point profiles were measured at fasting, 1 hour post morning meal, 2 hours post morning meal, pre midday meal, 1 hour post midday meal, 2 hours post midday meal, pre evening meal, 1 hour post evening meal, 2 hours post evening meal, and bedtime. LS Mean 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.

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

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As 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 values	Insulin Lispro (Humalog)	LY900014	LY900014 Postmeal	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	300	314	230	
Units: mg/dL				
least squares mean (standard error)				
Morning Premeal	-3.3 (± 2.84)	-1.1 (± 2.82)	2.9 (± 3.19)	
Morning 1-hour Postmeal	-1.0 (± 3.31)	-14.8 (± 3.30)	5.4 (± 3.71)	
Morning 2-hour Postmeal	1.4 (± 3.22)	-10.1 (± 3.21)	-0.2 (± 3.63)	
Midday Premeal	1.9 (± 2.83)	6.6 (± 2.80)	4.0 (± 3.17)	
Midday 1-hour Postmeal	1.4 (± 3.40)	-2.2 (± 3.36)	11.4 (± 3.81)	
Midday 2-hour Postmeal	-2.7 (± 3.28)	-5.2 (± 3.24)	0.0 (± 3.67)	
Evening Premeal	-1.4 (± 3.24)	5.2 (± 3.21)	0.4 (± 3.64)	
Evening 1-hour Postmeal	-0.9 (± 3.57)	-7.0 (± 3.53)	15.3 (± 3.95)	
Evening 2-hour Postmeal	-0.6 (± 3.45)	-8.2 (± 3.43)	-1.6 (± 3.83)	
Bedtime	-2.9 (± 3.56)	-6.8 (± 3.58)	-11.0 (± 4.08)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Insulin Dose

End point title	Change from Baseline in Insulin Dose[8]

End point description:

LS Mean 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.

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

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As 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 values	Insulin Lispro (Humalog)	LY900014	LY900014 Postmeal	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	379	400	285	
Units: Units (U)/day				
least squares mean (standard error)				
Total Daily Insulin Dose	2.0 (± 0.73)	2.9 (± 0.72)	2.2 (± 0.83)	
Daily Basal Insulin Dose	0.9 (± 0.29)	1.0 (± 0.28)	1.2 (± 0.33)	
Daily Prandial Insulin Dose	0.9 (± 0.60)	1.5 (± 0.59)	1.0 (± 0.68)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline in Insulin Treatment Satisfaction Questionnaire (ITSQ) Regimen Inconvenience Domain Score[9]

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. LS Mean was calculated using the ANCOVA model with last observation carried forward (LOCF) 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. The analysis included data prior to permanent discontinuation of study drug.

APD: All randomized participants with baseline and post-baseline data. Missing endpoints were imputed by applying the Last Observation Carried Forward (LOCF) method to post-baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 26

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As 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 values	Insulin Lispro (Humalog)	LY900014	LY900014 Postmeal	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	423	432	314	
Units: Units on a scale				
least squares mean (standard error)	0.7 (± 0.91)	1.4 (± 0.92)	1.5 (± 1.01)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in ITSQ Lifestyle Flexibility DomainScore

End point title	Change from Baseline in ITSQ Lifestyle Flexibility

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. LS Mean was calculated using the analysis of covariance (ANCOVA) model with LOCF 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. The analysis included data prior to permanent discontinuation of study drug.

APD: All randomized participants with baseline and post-baseline data. Missing endpoints were imputed by applying the LOCF method to the post-baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 26

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As 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 values	Insulin Lispro (Humalog)	LY900014	LY900014 Postmeal	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	423	432	314	
Units: Units on a scale				
least squares mean (standard error)	1.3 (± 1.07)	2.1 (± 1.09)	3.7 (± 1.19)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HbA1c <7%

End point title	Percentage of Participants with HbA1c <7%[11]

End point description:

Hemoglobin A1c (HbA1c) is the glycosylated fraction of hemoglobin A. HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time.

APD: All participants with baseline and one 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

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As 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 values	Insulin Lispro (Humalog)	LY900014	LY900014 Postmeal	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	442	450	322	
Units: Percentage of participants				
number (not applicable)	33.94	36.00	24.84	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HbA1c

End point title	Change from Baseline in HbA1c[12]

End point description:

HbA1c is the glycosylated fraction of hemoglobin A. HbA1c is measured to identify average plasma glucose concentration over prolonged periods of time.
Least Squares (LS) mean was determined by MMRM model with variables of baseline, pooled country, type of basal insulin during lead-in, prandial Insulin Dosing Plan, treatment (Type III sum of squares) as fixed factors.

APD: All randomized participants who received at least one dose of study drug and have at least one baseline and postbaseline observation for HbA1c. 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	Secondary

End point timeframe:

Baseline, Week 52

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As 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 values	Insulin Lispro (Humalog)	LY900014		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	400	410		
Units: Percentage of HbA1c				
least squares mean (standard error)	0.20 (± 0.037)	0.13 (± 0.036)		

Statistical analyses

Statistical analysis title	Change From Baseline in HbA1c (Week 52)
Comparison groups	Insulin Lispro (Humalog) v LY900014
Number of subjects included in analysis	810
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.184
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.03

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
I8B-MC-ITRM	
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	LY900014 Postmeal
Reporting group description: -	
Reporting group title	Insulin Lispro (Humalog) Lead-in-MEE
Reporting group description: -	
Reporting group title	Insulin Lispro (Humalog)-MEE
Reporting group description: -	
Reporting group title	LY900014-MEE
Reporting group description: -	
Reporting group title	LY900014 Postmeal-MEE
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	48 / 1316 (3.65%)	67 / 442 (15.16%)	54 / 451 (11.97%)
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)			
colon cancer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
ependymoma			
alternative dictionary used:			

MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
intraductal proliferative breast lesion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lipoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
Vascular disorders			
aortic stenosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	2 / 442 (0.45%)	0 / 451 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pregnancy, puerperium and perinatal conditions			
abortion missed			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[1]	0 / 573 (0.00%)	0 / 186 (0.00%)	0 / 201 (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
abortion spontaneous			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[2]	0 / 573 (0.00%)	0 / 186 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ectopic pregnancy			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed[3]	0 / 573 (0.00%)	0 / 186 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pre-eclampsia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[4]	0 / 573 (0.00%)	1 / 186 (0.54%)	0 / 201 (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
General disorders and administration site conditions			
death			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
non-cardiac chest pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
Reproductive system and breast disorders			
cervical dysplasia			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed[5]	0 / 573 (0.00%)	1 / 186 (0.54%)	0 / 201 (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
uterine polyp			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[6]	0 / 573 (0.00%)	0 / 186 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 1316 (0.08%)	0 / 442 (0.00%)	0 / 451 (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
lung disorder			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumothorax			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
depression			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
sleep disorder			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 1316 (0.15%)	2 / 442 (0.45%)	0 / 451 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bladder injury			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
brachial plexus injury			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 1316 (0.08%)	0 / 442 (0.00%)	0 / 451 (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
femoral neck fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
femur fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
foot fracture			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 1316 (0.08%)	1 / 442 (0.23%)	0 / 451 (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
injury			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
joint dislocation			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ligament rupture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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 injuries			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pelvic fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
radius fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	2 / 451 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

rib fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
road traffic accident			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 1316 (0.08%)	0 / 442 (0.00%)	0 / 451 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spinal compression fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
thermal burn			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
upper limb fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
wrist fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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	1 / 1316 (0.08%)	0 / 442 (0.00%)	0 / 451 (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
bradycardia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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 disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myocardial infarction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
palpitations			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

pericardial effusion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pericarditis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulseless electrical activity			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dural arteriovenous fistula			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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
headache			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hemiparesis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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 seizure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoglycaemic unconsciousness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 1316 (0.15%)	0 / 442 (0.00%)	2 / 451 (0.44%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ischaemic stroke			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
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 sclerosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
partial seizures			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 1316 (0.08%)	0 / 442 (0.00%)	0 / 451 (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

syncope			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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
transient ischaemic attack			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 1316 (0.08%)	2 / 442 (0.45%)	0 / 451 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
deafness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tinnitus			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
keratitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
impaired gastric emptying			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
oesophagitis			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 1316 (0.08%)	0 / 442 (0.00%)	0 / 451 (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
vomiting			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 1316 (0.08%)	0 / 442 (0.00%)	0 / 451 (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			
nephrolithiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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 colic			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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			
intervertebral disc protrusion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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
joint ankylosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rhabdomyolysis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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			
appendicitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 1316 (0.08%)	1 / 442 (0.23%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 1316 (0.08%)	1 / 442 (0.23%)	0 / 451 (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
epididymitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[7]	0 / 743 (0.00%)	1 / 256 (0.39%)	0 / 250 (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
erysipelas			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastroenteritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
genital herpes			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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
influenza			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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
localised infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteomyelitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peritonsillar abscess			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia streptococcal			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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

pyelonephritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 1316 (0.08%)	0 / 442 (0.00%)	0 / 451 (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
pyelonephritis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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 / 1316 (0.08%)	0 / 442 (0.00%)	0 / 451 (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
urogenital infection bacterial			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (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
viral pericarditis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	1 / 451 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
diabetes mellitus inadequate control			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	0 / 451 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diabetic ketoacidosis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 1316 (0.08%)	1 / 442 (0.23%)	0 / 451 (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
hypoglycaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	33 / 1316 (2.51%)	39 / 442 (8.82%)	33 / 451 (7.32%)
occurrences causally related to treatment / all	18 / 38	48 / 69	29 / 52
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ketoacidosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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
type 1 diabetes mellitus			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	0 / 442 (0.00%)	0 / 451 (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

Serious adverse events	LY900014 Postmeal	Insulin Lispro (Humalog) Lead-in-MEE	Insulin Lispro (Humalog)-MEE
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 329 (9.12%)	0 / 76 (0.00%)	9 / 31 (29.03%)
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)			
colon cancer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
ependymoma			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
intraductal proliferative breast lesion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
lipoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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			
aortic stenosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
Pregnancy, puerperium and perinatal conditions			
abortion missed			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[1]	1 / 147 (0.68%)	0 / 36 (0.00%)	0 / 14 (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
abortion spontaneous			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[2]	1 / 147 (0.68%)	0 / 36 (0.00%)	0 / 14 (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
ectopic pregnancy			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed[3]	0 / 147 (0.00%)	0 / 36 (0.00%)	0 / 14 (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
pre-eclampsia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[4]	0 / 147 (0.00%)	0 / 36 (0.00%)	0 / 14 (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			
death			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
non-cardiac chest pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
pyrexia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
Reproductive system and breast disorders			
cervical dysplasia			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed[5]	0 / 147 (0.00%)	0 / 36 (0.00%)	0 / 14 (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
uterine polyp			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[6]	0 / 147 (0.00%)	0 / 36 (0.00%)	0 / 14 (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			
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
lung disorder			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
pneumothorax			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
Psychiatric disorders			
depression			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (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
sleep disorder			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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			
ankle fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
bladder injury			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
brachial plexus injury			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
femoral neck fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
femur fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
foot fracture			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
joint dislocation			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 rupture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	1 / 31 (3.23%)
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 injuries			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
pelvic fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
radius fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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

rib fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
road traffic accident			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
thermal burn			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
upper limb fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
wrist fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 pectoris			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (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
angina unstable			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (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
bradycardia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
palpitations			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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

pericardial effusion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
pericarditis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
pulseless electrical activity			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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			
dizziness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
dural arteriovenous fistula			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (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
headache			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
hemiparesis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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	2 / 329 (0.61%)	0 / 76 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoglycaemic seizure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoglycaemic unconsciousness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
ischaemic stroke			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 sclerosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
partial seizures			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (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
transient ischaemic attack			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (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
Ear and labyrinth disorders			
deafness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
tinnitus			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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			
keratitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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			
impaired gastric emptying			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
oesophagitis			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
vomiting			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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			
nephrolithiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (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 colic			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (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
Musculoskeletal and connective tissue disorders			
intervertebral disc protrusion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
joint ankylosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
rhabdomyolysis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 329 (0.61%)	0 / 76 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
epididymitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[7]	0 / 182 (0.00%)	0 / 40 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
erysipelas			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
genital herpes			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (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
influenza			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (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
localised infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
peritonsillar abscess			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 streptococcal			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

pyelonephritis alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 / 329 (0.00%)	0 / 76 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
urogenital infection bacterial alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
viral pericarditis alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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 diabetes mellitus inadequate control alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	0 / 31 (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
diabetic ketoacidosis alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	2 / 31 (6.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoglycaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	16 / 329 (4.86%)	0 / 76 (0.00%)	3 / 31 (9.68%)
occurrences causally related to treatment / all	12 / 23	0 / 0	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ketoacidosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (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
type 1 diabetes mellitus			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	LY900014-MEE	LY900014 Postmeal-MEE	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 21 (14.29%)	2 / 22 (9.09%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
colon cancer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ependymoma			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
intraductal proliferative breast lesion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
lipoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
aortic stenosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
abortion missed			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[1]	0 / 9 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
abortion spontaneous			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[2]	0 / 9 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ectopic pregnancy			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed[3]	0 / 9 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pre-eclampsia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[4]	0 / 9 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
death			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
non-cardiac chest pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pyrexia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
drug hypersensitivity			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
cervical dysplasia			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed[5]	0 / 9 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
uterine polyp			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[6]	0 / 9 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
lung disorder			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumothorax			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
depression			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
sleep disorder			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bladder injury			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
brachial plexus injury			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
femoral neck fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
femur fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
foot fracture			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
injury			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
joint dislocation			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ligament rupture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
multiple injuries			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pelvic fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
radius fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

rib fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
road traffic accident			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal compression fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
thermal burn			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper limb fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
wrist fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
angina pectoris			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
angina unstable			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bradycardia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
coronary artery disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocardial infarction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
palpitations			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

pericardial effusion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pericarditis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulseless electrical activity			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dural arteriovenous fistula			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
headache			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hemiparesis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoglycaemic coma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoglycaemic seizure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoglycaemic unconsciousness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ischaemic stroke			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
multiple sclerosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
partial seizures			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

syncope			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
transient ischaemic attack			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
deafness			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
tinnitus			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
keratitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
impaired gastric emptying			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
oesophagitis			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
vomiting			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
nephrolithiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal colic			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
intervertebral disc protrusion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
joint ankylosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
rhabdomyolysis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
epididymitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[7]	0 / 12 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
erysipelas			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastroenteritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
genital herpes			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
influenza			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
localised infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
osteomyelitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
peritonsillar abscess			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia streptococcal			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

pyelonephritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pyelonephritis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
urogenital infection bacterial			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
viral pericarditis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
diabetes mellitus inadequate control			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diabetic ketoacidosis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoglycaemia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	3 / 21 (14.29%)	2 / 22 (9.09%)	
occurrences causally related to treatment / all	4 / 6	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
ketoacidosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
type 1 diabetes mellitus			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
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: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of

subjects exposed has been adjusted accordingly.

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

Non-serious adverse events	Insulin Lispro (Humalog) Lead-in	Insulin Lispro (Humalog)	LY900014
Total subjects affected by non-serious adverse events			
subjects affected / exposed	131 / 1316 (9.95%)	147 / 442 (33.26%)	163 / 451 (36.14%)
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 1316 (0.00%)	1 / 442 (0.23%)	1 / 451 (0.22%)
occurrences (all)	0	1	1
maternal exposure during pregnancy			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[8]	2 / 573 (0.35%)	3 / 186 (1.61%)	2 / 201 (1.00%)
occurrences (all)	2	3	2
Surgical and medical procedures			
vasectomy			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[9]	0 / 743 (0.00%)	0 / 256 (0.00%)	0 / 250 (0.00%)
occurrences (all)	0	0	0
Pregnancy, puerperium and perinatal conditions			
hyperemesis gravidarum			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[10]	0 / 573 (0.00%)	0 / 186 (0.00%)	0 / 201 (0.00%)
occurrences (all)	0	0	0
placenta praevia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[11]	0 / 573 (0.00%)	0 / 186 (0.00%)	0 / 201 (0.00%)
occurrences (all)	0	0	0
retroplacental haematoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[12]	0 / 573 (0.00%)	0 / 186 (0.00%)	0 / 201 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

pyrexia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	4 / 1316 (0.30%)	2 / 442 (0.45%)	6 / 451 (1.33%)
occurrences (all)	4	2	7
Reproductive system and breast disorders			
vaginal haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[13]	1 / 573 (0.17%)	0 / 186 (0.00%)	1 / 201 (0.50%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	9 / 1316 (0.68%)	4 / 442 (0.90%)	7 / 451 (1.55%)
occurrences (all)	9	5	7
Musculoskeletal and connective tissue disorders			
pain in extremity			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 1316 (0.08%)	5 / 442 (1.13%)	4 / 451 (0.89%)
occurrences (all)	1	5	5
Infections and infestations			
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 1316 (0.08%)	2 / 442 (0.45%)	1 / 451 (0.22%)
occurrences (all)	1	2	1
influenza			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	5 / 1316 (0.38%)	24 / 442 (5.43%)	24 / 451 (5.32%)
occurrences (all)	5	24	25
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	85 / 1316 (6.46%)	88 / 442 (19.91%)	106 / 451 (23.50%)
occurrences (all)	87	123	161
pharyngitis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	3 / 1316 (0.23%)	4 / 442 (0.90%)	6 / 451 (1.33%)
occurrences (all)	3	5	6
upper respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	25 / 1316 (1.90%)	33 / 442 (7.47%)	28 / 451 (6.21%)
occurrences (all)	25	43	34

Non-serious adverse events	LY900014 Postmeal	Insulin Lispro (Humalog) Lead-in-MEE	Insulin Lispro (Humalog)-MEE
Total subjects affected by non-serious adverse events			
subjects affected / exposed	104 / 329 (31.61%)	5 / 76 (6.58%)	13 / 31 (41.94%)
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 329 (0.00%)	0 / 76 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
maternal exposure during pregnancy			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[8]	2 / 147 (1.36%)	0 / 36 (0.00%)	1 / 14 (7.14%)
occurrences (all)	2	0	1
Surgical and medical procedures			
vasectomy			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[9]	0 / 182 (0.00%)	0 / 40 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Pregnancy, puerperium and perinatal conditions			
hyperemesis gravidarum			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[10]	0 / 147 (0.00%)	0 / 36 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
placenta praevia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[11]	0 / 147 (0.00%)	0 / 36 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
retroplacental haematoma			
alternative dictionary used:			

MedDRA 21.1			
subjects affected / exposed[12]	0 / 147 (0.00%)	0 / 36 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
pyrexia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	8 / 329 (2.43%)	2 / 76 (2.63%)	4 / 31 (12.90%)
occurrences (all)	8	2	4
Reproductive system and breast disorders			
vaginal haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[13]	0 / 147 (0.00%)	0 / 36 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	6 / 329 (1.82%)	0 / 76 (0.00%)	2 / 31 (6.45%)
occurrences (all)	6	0	2
Musculoskeletal and connective tissue disorders			
pain in extremity			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	1 / 76 (1.32%)	2 / 31 (6.45%)
occurrences (all)	1	1	2
Infections and infestations			
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 329 (0.30%)	0 / 76 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
influenza			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	15 / 329 (4.56%)	1 / 76 (1.32%)	3 / 31 (9.68%)
occurrences (all)	16	1	4
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	66 / 329 (20.06%)	1 / 76 (1.32%)	5 / 31 (16.13%)
occurrences (all)	85	1	7
pharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	4 / 329 (1.22%)	0 / 76 (0.00%)	2 / 31 (6.45%)
occurrences (all)	5	0	2
upper respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	19 / 329 (5.78%)	1 / 76 (1.32%)	1 / 31 (3.23%)
occurrences (all)	22	1	1

Non-serious adverse events	LY900014-MEE	LY900014 Postmeal-MEE	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 21 (14.29%)	4 / 22 (18.18%)	
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
maternal exposure during pregnancy			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[8]	0 / 9 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Surgical and medical procedures			
vasectomy			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[9]	0 / 12 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Pregnancy, puerperium and perinatal conditions			
hyperemesis gravidarum			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[10]	0 / 9 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
placenta praevia			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed[11]	0 / 9 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
retroplacental haematoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[12]	0 / 9 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
pyrexia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
vaginal haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[13]	0 / 9 (0.00%)	0 / 13 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
pain in extremity			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
influenza			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 21 (4.76%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
pharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
upper respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	

Notes:

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.
[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 May 2017	-Immunogenicity follow-up shortened. -The primary analysis was 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: