



## Clinical trial results:

### The Impact of LY2605541 versus Insulin Glargine for Patients with Type 1 Diabetes Mellitus Treated with Preprandial Insulin Lispro: An Open-Label, Randomized, 78-Week Study - The IMAGINE 1 Study

#### Summary

EudraCT number	2011-001261-40
Trial protocol	DE AT IT
Global end of trial date	07 June 2014

#### Results information

Result version number	v1 (current)
This version publication date	02 April 2018
First version publication date	02 April 2018

#### Trial information

##### Trial identification

Sponsor protocol code	I2R-MC-BIAN
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01481779
WHO universal trial number (UTN)	-
Other trial identifiers	Eli Lilly and Company: 12146

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	07 June 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	07 June 2014
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that glycemic control, as measured by HbA1c at 26 weeks, for insulin peglispro was noninferior compared with insulin glargine when each was combined with preprandial insulin lispro in patients with type 1 diabetes mellitus (T1DM).

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	06 January 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	France: 37
Country: Number of subjects enrolled	United States: 130
Country: Number of subjects enrolled	Mexico: 40
Country: Number of subjects enrolled	Poland: 41
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Germany: 66
Country: Number of subjects enrolled	Japan: 91
Country: Number of subjects enrolled	Italy: 19
Worldwide total number of subjects	455
EEA total number of subjects	174

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)	439
From 65 to 84 years	16
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Study included a 2-3 week screening period, a 78-week treatment period (26-week primary endpoint assessment, followed by a 52-week extension), and a 4-week post treatment follow-up period.

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	LY2605541 + Insulin Lispro

Arm description:

LY2605541 titrated based on blood glucose readings, administered by subcutaneous (SC) injection via pen device once daily at bedtime for 78 weeks in combination with Insulin Lispro. Insulin Lispro titrated based on blood glucose readings, administered by SC injection via pen device at meal times for 78 weeks.

Arm type	Experimental
Investigational medicinal product name	LY2605541
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

LY2605541 titrated based on blood glucose readings, administered by subcutaneous (SC) injection via pen device once daily at bedtime for 78 weeks

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin Lispro titrated based on blood glucose readings, administered by SC injection via pen device at meal times for 78 weeks.

<b>Arm title</b>	Glargine + Insulin Lispro
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Arm description:

Glargine dose titrated based on blood glucose readings, administered by SC injection via pen device once daily at bedtime for 78 weeks in combination with Insulin Lispro. Insulin Lispro dose titrated based on blood glucose readings, administered by SC injection via pen device at meal times for 78 weeks.

Arm type	Active comparator
Investigational medicinal product name	Glargine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Glargine dose titrated based on blood glucose readings, administered by SC injection via pen device

once daily at bedtime for 78 weeks.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin Lispro titrated based on blood glucose readings, administered by SC injection via pen device at meal times for 78 weeks.

<b>Number of subjects in period 1</b>	<b>LY2605541 + Insulin Lispro</b>	<b>Glargine + Insulin Lispro</b>
Started	295	160
Received at Least 1 Dose of Study Drug	294	159
Completed	225	132
Not completed	70	28
Consent withdrawn by subject	26	13
Physician decision	13	4
Adverse event, non-fatal	23	5
Sponsor Decision	3	1
Lost to follow-up	3	2
Protocol deviation	2	3

## Baseline characteristics

### Reporting groups

Reporting group title	LY2605541 + Insulin Lispro
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Reporting group description:

LY2605541 titrated based on blood glucose readings, administered by subcutaneous (SC) injection via pen device once daily at bedtime for 78 weeks in combination with Insulin Lispro. Insulin Lispro titrated based on blood glucose readings, administered by SC injection via pen device at meal times for 78 weeks.

Reporting group title	Glargine + Insulin Lispro
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Reporting group description:

Glargine dose titrated based on blood glucose readings, administered by SC injection via pen device once daily at bedtime for 78 weeks in combination with Insulin Lispro. Insulin Lispro dose titrated based on blood glucose readings, administered by SC injection via pen device at meal times for 78 weeks.

Reporting group values	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro	Total
Number of subjects	295	160	455
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age Continuous			
Units: years			
arithmetic mean	39.68	38.91	
standard deviation	± 12.93	± 14.1	-
Gender, Male/Female			
Units:			
Female	157	73	230
Male	138	87	225
Region of Enrollment			
Units: Subjects			
France	23	14	37
United States	85	45	130
Mexico	25	15	40
Poland	27	14	41
Austria	7	4	11
Russian Federation	11	9	20
Germany	45	21	66
Japan	60	31	91
Italy	12	7	19
Ethnicity			
Units: Subjects			

Hispanic or Latino	33	16	49
Not Hispanic or Latino	153	85	238
Unknown or Not Reported	109	59	168
<b>Race</b>			
Units: Subjects			
American Indian or Alaska Native	6	3	9
Asian	63	31	94
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	5	0	5
White	221	125	346
More than one race	0	1	1
Unknown or Not Reported	0	0	0

## End points

### End points reporting groups

Reporting group title	LY2605541 + Insulin Lispro
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Reporting group description:

LY2605541 titrated based on blood glucose readings, administered by subcutaneous (SC) injection via pen device once daily at bedtime for 78 weeks in combination with Insulin Lispro. Insulin Lispro titrated based on blood glucose readings, administered by SC injection via pen device at meal times for 78 weeks.

Reporting group title	Glargine + Insulin Lispro
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Reporting group description:

Glargine dose titrated based on blood glucose readings, administered by SC injection via pen device once daily at bedtime for 78 weeks in combination with Insulin Lispro. Insulin Lispro dose titrated based on blood glucose readings, administered by SC injection via pen device at meal times for 78 weeks.

### Primary: Hemoglobin A1c (HbA1c) at 26 weeks

End point title	Hemoglobin A1c (HbA1c) at 26 weeks <sup>[1]</sup>
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End point description:

HbA1c is a test that measures a participant's average blood glucose level over a 2- to 3-month timeframe. Least Squares (LS) means were calculated using mixed model repeated measures (MMRM), adjusting for treatment, stratification factors (baseline low-density lipoprotein cholesterol [LDL-C] [ $<100$  milligrams per deciliter (mg/dL) and  $\geq 100$  mg/dL] and country), visit, treatment-by-visit interaction, and baseline HbA1c as the fixed effects and participant as the random effect.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable HbA1c data at both baseline and post-baseline.

End point type	Primary
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End point timeframe:

26 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No inferential statistics were planned or conducted for this endpoint.

End point values	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	153		
Units: percentage of HbA1c				
least squares mean (standard error)	7.06 ( $\pm$ 0.04)	7.43 ( $\pm$ 0.06)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Hemoglobin A1c (HbA1c)

End point title	Hemoglobin A1c (HbA1c)
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End point description:

HbA1c is a test that measures a participant's average blood glucose level over a 2- to 3-month timeframe. LS means were calculated using MMRM, adjusting for treatment, stratification factors

(baseline LDL-C [ $<100$  mg/dL and  $\geq 100$  mg/dL] and country), visit, treatment-by-visit interaction, and baseline HbA1c as the fixed effects.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable HbA1c data at both baseline and post-baseline.

End point type	Secondary
End point timeframe:	
52 weeks and 78 weeks	

End point values	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	153		
Units: percentage of HbA1c				
least squares mean (standard error)				
Week 52	7.3 ( $\pm 0.05$ )	7.55 ( $\pm 0.06$ )		
Week 78	7.43 ( $\pm 0.05$ )	7.7 ( $\pm 0.07$ )		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with hemoglobin A1c (HbA1c) less than 7.0% or less than or equal to 6.5% using last observation carried forward (LOCF)

End point title	Percentage of participants with hemoglobin A1c (HbA1c) less than 7.0% or less than or equal to 6.5% using last observation carried forward (LOCF)
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End point description:

HbA1c is a test that measures a participant's average blood glucose level over a 2- to 3-month timeframe. The percentage of participants was calculated by dividing the number of participants reaching target HbA1c by the total number of participants analyzed, then multiplying by 100.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable HbA1c data. Missing endpoints were imputed with the LOCF method, using only post-baseline data.

End point type	Secondary
End point timeframe:	
26 weeks and 52 weeks and 78 weeks	

End point values	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	153		
Units: percentage of participants				
number (not applicable)				
HbA1c $\leq 6.5\%$ , Week 26	28.6	13.7		
HbA1c $\leq 6.5\%$ , Week 52	23.3	13.1		
HbA1c $\leq 6.5\%$ , Week 78	20.2	13.1		

HbA1c <7.0%, Week 26	44.9	27.5		
HbA1c <7.0%, Week 52	37.3	28.1		
HbA1c <7.0%, Week 78	34.5	22.9		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in Hemoglobin A1c (HbA1c)

End point title	Change from baseline in Hemoglobin A1c (HbA1c)
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End point description:

HbA1c is a test that measures a participant's average blood glucose level over a 2- to 3-month timeframe. LS means were calculated using MMRM, adjusting for treatment, stratification factors (baseline LDL-C [ $<100$  mg/dL and  $\geq 100$  mg/dL] and country), visit, treatment-by-visit interaction, and baseline HbA1c as the fixed effects.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable HbA1c data at both baseline and post-baseline.

End point type	Secondary
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End point timeframe:

Baseline, 26 weeks, 52 weeks, 78 weeks

End point values	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	153		
Units: percentage of HbA1c				
least squares mean (standard error)				
Week 26	-0.69 ( $\pm 0.04$ )	-0.33 ( $\pm 0.06$ )		
Week 52	-0.46 ( $\pm 0.05$ )	-0.21 ( $\pm 0.06$ )		
Week 78	-0.33 ( $\pm 0.05$ )	-0.05 ( $\pm 0.07$ )		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Proportion of participants with hemoglobin A1c (HbA1c) less than 7.0% without nocturnal hypoglycemia

End point title	Proportion of participants with hemoglobin A1c (HbA1c) less than 7.0% without nocturnal hypoglycemia
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End point description:

Hypoglycemic episodes are defined as an event that is associated with reported signs and symptoms of hypoglycemia and/or a documented blood glucose concentration of  $\leq 70$  mg/dL (3.9 millimoles per liter [mmol/L]). A nocturnal hypoglycemic event occurred between bedtime and waking and between the time points of 10:00 PM and 10:00 AM. The percentage of participants was calculated by dividing the number of participants with HbA1c <7.0% without nocturnal hypoglycemia by the total number of participants analyzed, then multiplying by 100.

Participants who were randomized, had at least 1 dose of study medication, and had evaluable data. Missing endpoints were imputed with the LOCF method.

End point type	Secondary
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End point timeframe:

26 weeks and 52 weeks and 78 weeks

<b>End point values</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	153		
Units: percentage of participants				
number (not applicable)				
Week 26	3.8	2		
Week 52	2.1	0.7		
Week 78	1	0		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Total hypoglycemia rates (Adjusted by 30 days)

End point title	Total hypoglycemia rates (Adjusted by 30 days)
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End point description:

Hypoglycemic episodes are defined as events that are associated with reported signs and symptoms of hypoglycemia and/or documented blood glucose (BG) concentrations of  $\leq 70$  mg/dL (3.9 mmol/L). Group mean rates of total hypoglycemia (per 30 days) are presented and were calculated from negative binomial regression models (number of episodes = treatment + baseline total hypoglycemia rate, with log [exposure in days/30] as an offset variable). Group mean is estimated by taking the inverse link function on individual participant covariates first and then averages over all participants.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable data at both baseline and post-baseline.

End point type	Secondary
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End point timeframe:

Baseline through 26 weeks and Baseline through 52 weeks and Baseline through 78 weeks

<b>End point values</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	159		
Units: episodes/participant/30 days				
arithmetic mean (standard error)				
Baseline-Week 26	16.01 ( $\pm$ 0.44)	12.43 ( $\pm$ 0.55)		
Baseline-Week 52	14.84 ( $\pm$ 0.42)	11.75 ( $\pm$ 0.55)		
Baseline-Week 78	14.33 ( $\pm$ 0.42)	11.43 ( $\pm$ 0.55)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with total hypoglycemia events

End point title | Percentage of participants with total hypoglycemia events

End point description:

Hypoglycemic events are defined as events that are associated with reported signs and symptoms of hypoglycemia and/or documented BG concentrations of  $\leq 70$  mg/dL (3.9 mmol/L). The percentage of participants was calculated by dividing the number of participants with hypoglycemic episodes by the total number of participants analyzed, then multiplying by 100.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable data at both baseline and post-baseline.

End point type | Secondary

End point timeframe:

Baseline through 26 weeks and Baseline through 52 weeks and Baseline through 78 weeks

End point values	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	159		
Units: percentage of participants				
number (not applicable)				
Baseline-Week 26	99	96.9		
Baseline-Week 52	99	96.9		
Baseline-Week 78	99	96.9		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with nocturnal hypoglycemic Events

End point title | Percentage of participants with nocturnal hypoglycemic Events

End point description:

Hypoglycemic episodes are defined as an event that is associated with reported signs and symptoms of hypoglycemia and/or a BG concentration of  $\leq 70$  mg/dL (3.9 mmol/L). A nocturnal hypoglycemic event occurred between bedtime and waking and between the time points of 10:00 PM and 10:00 AM. The percentage of participants was calculated by dividing the number of participants with nocturnal hypoglycemic episodes by the total number of participants analyzed, then multiplying by 100.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable data at both baseline and post-baseline.

End point type | Secondary

End point timeframe:

Baseline through 26 weeks and Baseline through 52 weeks and Baseline through 78 weeks

<b>End point values</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	159		
Units: percentage of participants				
number (not applicable)				
Baseline-Week 26	87.4	90.6		
Baseline-Week 52	91.5	91.8		
Baseline-Week 78	93.5	92.5		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Nocturnal hypoglycemia rates (Adjusted by 30 days)

End point title | Nocturnal hypoglycemia rates (Adjusted by 30 days)

End point description:

Hypoglycemic episodes are defined as events that are associated with reported signs and symptoms of hypoglycemia and/or a documented BG concentration of  $\leq 70$  mg/dL (3.9 mmol/L). A nocturnal hypoglycemic event occurred between bedtime and waking and between the time points of 10:00 PM and 10:00 AM. Group mean rates of nocturnal hypoglycemia (per 30 days) are presented and were calculated from negative binomial regression models (number of episodes = treatment + baseline nocturnal hypoglycemia rate, with  $\log$  [exposure in days/30] as an offset variable). Group mean is estimated by taking the inverse link function on individual participant covariates first and then averages over all participants.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable data at both baseline and post-baseline.

End point type | Secondary

End point timeframe:

Baseline through 26 weeks and Baseline through 52 weeks and Baseline through 78 weeks

<b>End point values</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	159		
Units: episodes/participant/30 days				
arithmetic mean (standard error)				
Baseline-Week 26	1.69 ( $\pm$ 0.12)	2.66 ( $\pm$ 0.19)		
Baseline-Week 52	1.63 ( $\pm$ 0.11)	2.45 ( $\pm$ 0.19)		
Baseline-Week 78	1.58 ( $\pm$ 0.11)	2.28 ( $\pm$ 0.17)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Fasting serum glucose (FSG) by laboratory measurement

End point title Fasting serum glucose (FSG) by laboratory measurement

End point description:

LS means were calculated using MMRM, adjusting for treatment, stratification factors (baseline HbA1c [ $\leq 8.5\%$  and  $> 8.5\%$ ], baseline LDL-C level [ $< 100$  mg/dL and  $\geq 100$  mg/dL], and country), visit, treatment-by-visit interaction, and corresponding baseline dependent variable as the fixed effects, and participants as the random effect.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable FSG data at both baseline and post-baseline.

End point type Secondary

End point timeframe:

26 weeks and 52 weeks and 78 weeks

End point values	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	285	152		
Units: mg/dL				
least squares mean (standard error)				
Week 26	138.22 ( $\pm 3.8$ )	160.35 ( $\pm 5.06$ )		
Week 52	146.55 ( $\pm 4.42$ )	164.28 ( $\pm 5.72$ )		
Week 78	144.64 ( $\pm 4.53$ )	164.78 ( $\pm 5.81$ )		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Fasting blood glucose (FBG) intra-participant variability

End point title Fasting blood glucose (FBG) intra-participant variability

End point description:

FBG was measured by self-monitored blood glucose (SMBG). Between-day glucose variability is measured by the standard deviation of FBG. LS means were calculated using MMRM, adjusting for treatment, stratification factors (baseline HbA1c [ $\leq 8.5\%$  and  $> 8.5\%$ ], baseline LDL-C level [ $< 100$  mg/dL and  $\geq 100$  mg/dL], and country), visit, treatment-by-visit interaction, and corresponding baseline dependent variable as the fixed effects, and participants as the random effect.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable FBG data at both baseline and post-baseline.

End point type	Secondary
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End point timeframe:

26 weeks and 52 weeks and 78 weeks

<b>End point values</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	282	153		
Units: mg/dL				
least squares mean (standard error)				
Week 26	52.49 (± 1.79)	59.25 (± 2.43)		
Week 52	53.44 (± 1.85)	58.15 (± 2.43)		
Week 78	54.87 (± 2.2)	60.66 (± 2.79)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: 9 point self-monitored blood glucose (SMBG)

End point title	9 point self-monitored blood glucose (SMBG)
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End point description:

9-point SMBG profiles were obtained over 2 days within the week prior to Weeks 0, 4, 12, 26, 39, 52, 65, and 78. SMBG measurements were taken at 9 time points: pre-morning meal, 2 hours post-morning meal, pre-midday meal, 2 hours post-midday meal, pre-evening meal, 2 hours post-evening meal, bedtime, at approximately 0300 hours, and the pre-morning meal the next day. LS means were calculated using MMRM, adjusting for treatment, stratification factors (baseline HbA1c [ $\leq 8.5\%$  and  $>8.5\%$ ], baseline LDL-C level [ $<100$  mg/dL and  $\geq 100$  mg/dL], and country), visit, treatment-by-visit interaction, and corresponding baseline dependent variable as the fixed effects and participants as the random effect.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable SMBG data at both baseline and post-baseline.

End point type	Secondary
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End point timeframe:

26 weeks and 52 weeks and 78 weeks

<b>End point values</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	271	143		
Units: mg/dL				
least squares mean (standard error)				
Pre-morning meal, Week 26 (n=271, 143)	158.58 (± 3.82)	144.4 (± 5.2)		
Pre-morning meal, Week 52 (n=271, 143)	160.89 (± 4.13)	152.55 (± 5.38)		

Pre-morning meal, Week 78 (n=271, 143)	163.09 (± 4.66)	153.38 (± 5.99)		
2 hours post-morning meal, Week 26 (n=245, 125)	172.39 (± 4.59)	165.53 (± 6.44)		
2 hours post-morning meal, Week 52 (n=245, 125)	176.32 (± 5.61)	168.38 (± 7.47)		
2 hours post-morning meal, Week 78 (n=245, 125)	183.64 (± 6.23)	190.54 (± 7.91)		
Pre-midday meal, Week 26 (n=264, 140)	136.21 (± 3.92)	153.12 (± 5.33)		
Pre-midday meal, Week 52 (n=264, 140)	142.82 (± 4.27)	149.78 (± 5.66)		
Pre-midday meal, Week 78 (n=264, 140)	150.83 (± 4.9)	154.56 (± 6.33)		
2 hours post-midday meal, Week 26 (n=244, 122)	157.17 (± 4.78)	164.75 (± 6.69)		
2 hours post-midday meal, Week 52 (n=244, 122)	159.59 (± 5.11)	168.83 (± 6.94)		
2 hours post-midday meal, Week 78 (n=244, 122)	154.46 (± 5.76)	175.52 (± 7.51)		
Pre-evening meal, Week 26 (n=266, 143)	153.2 (± 4.29)	168.08 (± 5.75)		
Pre-evening meal, Week 52 (n=266, 143)	153.01 (± 5.17)	183.18 (± 6.81)		
Pre-evening meal, Week 78 (n=266, 143)	149.89 (± 4.92)	174.5 (± 6.17)		
2 hours post-evening meal, Week 26 (n=232, 126)	149.74 (± 5.17)	191.99 (± 7.2)		
2 hours post-evening meal, Week 52 (n=232, 126)	157.81 (± 6.79)	198.1 (± 9.06)		
2 hours post-evening meal, Week 78 (n=232, 126)	163.27 (± 6.07)	189.43 (± 7.75)		
Bedtime, Week 26 (n=250, 137)	151.66 (± 4.15)	176.17 (± 5.63)		
Bedtime, Week 52 (n=250, 137)	167.35 (± 5.33)	182.08 (± 7.11)		
Bedtime, Week 78 (n=250, 137)	165.63 (± 5.37)	185.45 (± 6.74)		
0300 hours, Week 26 (n=219, 116)	159.73 (± 5.3)	163.18 (± 7.5)		
0300 hours, Week 52 (n=219, 116)	157.52 (± 6.06)	148.26 (± 8.36)		
0300 hours, Week 78 (n=219, 116)	165.82 (± 7.19)	170.35 (± 9.02)		
Pre-morning meal next day, Week 26 (n=260, 138)	149.94 (± 3.74)	143.89 (± 5.1)		
Pre-morning meal next day, Week 52 (n=260, 138)	155.79 (± 4.24)	145.55 (± 5.59)		
Pre-morning meal next day, Week 78 (n=260, 138)	156.87 (± 4.8)	152.63 (± 6.11)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: 0300-hour blood glucose (BG) to fasting blood (FBG) glucose excursion

End point title	0300-hour blood glucose (BG) to fasting blood (FBG) glucose excursion
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**End point description:**

Results of a 0300-hour to pre-morning meal (FBG) excursion are presented (only SMBG profiles with both 0300 hours and the next day pre-morning measurements are included for the calculation of such excursion). LS means were calculated using MMRM, adjusting for treatment, stratification factors (baseline HbA1c [ $\leq 8.5\%$  and  $> 8.5\%$ ], baseline LDL-C level [ $< 100$  mg/dL and  $\geq 100$  mg/dL], and country), visit, treatment-by-visit interaction, and corresponding baseline dependent variable as the fixed effects and participants as the random effect.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable SMBG data at baseline and post-baseline.

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End point type	Secondary
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End point timeframe:

26 weeks and 52 weeks and 78 weeks

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<b>End point values</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	112		
Units: mg/dL				
least squares mean (standard error)				
Week 26	-9.92 ( $\pm$ 6.24)	-14.08 ( $\pm$ 8.75)		
Week 52	-6.15 ( $\pm$ 6.91)	-9.02 ( $\pm$ 9.58)		
Week 78	-10.82 ( $\pm$ 8.25)	-28.94 ( $\pm$ 10.5)		

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Change from baseline in body weight**

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End point title	Change from baseline in body weight
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End point description:

LS means were calculated using MMRM, adjusting for treatment, stratification factors (baseline HbA1c [ $\leq 8.5\%$  and  $> 8.5\%$ ], baseline LDL-C level [ $< 100$  mg/dL and  $\geq 100$  mg/dL], and country), visit, treatment-by-visit interaction, and corresponding baseline dependent variable as the fixed effects, and participants as the random effect.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable body weight data at both baseline and post-baseline.

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End point type	Secondary
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End point timeframe:

Baseline and 26 weeks and 52 weeks and 78 weeks

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<b>End point values</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	154		
Units: kilograms (kg)				
least squares mean (standard error)				
Week 26	-1.17 (± 0.2)	0.71 (± 0.27)		
Week 52	-1.22 (± 0.25)	1 (± 0.33)		
Week 78	-0.93 (± 0.28)	1.04 (± 0.37)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Basal, bolus, and total insulin dose

End point title	Basal, bolus, and total insulin dose
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End point description:

Basal insulin dose, short-acting bolus insulin dose (each meal and overall), and total insulin dose were calculated based on the dose during the last 7 days prior to the post-treatment visit or last 3 days prior to the randomization visit. LS means were calculated using MMRM, adjusting for treatment, stratification factors (baseline HbA1c [ $\leq 8.5\%$  and  $> 8.5\%$ ], baseline LDL-C level [ $< 100$  mg/dL and  $\geq 100$  mg/dL], and country), visit, treatment-by-visit interaction, and corresponding baseline dependent variable as the fixed effects and participants as the random effect.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable insulin dose data.

End point type	Secondary
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End point timeframe:

26 weeks and 52 weeks and 78 weeks

<b>End point values</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	282	156		
Units: units/kg/day				
least squares mean (standard error)				
Basal Insulin, Week 26 (n=239, 127)	0.4 (± 0.01)	0.34 (± 0.01)		
Basal Insulin, Week 52 (n=239, 127)	0.4 (± 0.01)	0.34 (± 0.01)		
Basal Insulin, Week 78 (n=239, 127)	0.41 (± 0.01)	0.35 (± 0.01)		
Bolus Insulin, Week 26 (n=280, 153)	0.37 (± 0.01)	0.46 (± 0.02)		
Bolus Insulin, Week 52 (n=280, 153)	0.38 (± 0.01)	0.47 (± 0.02)		
Bolus Insulin, Week 78 (n=280, 153)	0.37 (± 0.02)	0.48 (± 0.02)		
Total Insulin, Week 26 (n=282, 156)	0.73 (± 0.02)	0.78 (± 0.02)		
Total Insulin, Week 52 (n=282, 156)	0.74 (± 0.02)	0.79 (± 0.03)		
Total Insulin, Week 78 (n=282, 156)	0.75 (± 0.02)	0.8 (± 0.03)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Lipid profile

End point title	Lipid profile
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End point description:

Concentrations of cholesterol, high-density lipoprotein cholesterol (HDL-C), LDL-C, and triglycerides are summarized. LS means were calculated using MMRM, adjusting for stratification factors (baseline HbA1c [ $\leq 8.5\%$  and  $> 8.5\%$ ], country, LDL-C [ $< 100$  mg/dL and  $\geq 100$  mg/dL] except for the LDL-C outcome variable), visit, treatment, treatment-by-visit interaction, and baseline value of corresponding lipid outcome variable.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable lipid data at both baseline and post-baseline.

End point type	Secondary
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End point timeframe:

26 weeks and 52 weeks and 78 weeks

End point values	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288	152		
Units: mg/dL				
least squares mean (standard error)				
Cholesterol, Week 26	191.86 ( $\pm$ 1.63)	187.93 ( $\pm$ 2.19)		
Cholesterol, Week 52	190.72 ( $\pm$ 1.59)	188.65 ( $\pm$ 2.1)		
Cholesterol, Week 78	191.78 ( $\pm$ 1.86)	190.06 ( $\pm$ 2.39)		
HDL-C, Week 26	61.87 ( $\pm$ 0.59)	62.75 ( $\pm$ 0.8)		
HDL-C, Week 52	61.01 ( $\pm$ 0.56)	61.46 ( $\pm$ 0.74)		
HDL-C, Week 78	60.77 ( $\pm$ 0.66)	61.97 ( $\pm$ 0.85)		
LDL-C, Week 26	108.85 ( $\pm$ 1.33)	108.31 ( $\pm$ 1.79)		
LDL-C, Week 52	109.4 ( $\pm$ 1.39)	109.74 ( $\pm$ 1.84)		
LDL-C, Week 78	109.62 ( $\pm$ 1.62)	110.35 ( $\pm$ 2.09)		
Triglycerides, Week 26	109.64 ( $\pm$ 3.89)	85.35 ( $\pm$ 5.24)		
Triglycerides, Week 52	105.17 ( $\pm$ 3.64)	87.94 ( $\pm$ 4.8)		
Triglycerides, Week 78	110.8 ( $\pm$ 4.78)	88.96 ( $\pm$ 6.14)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants with Change in anti-LY2605541 antibodies

End point title	Percentage of Participants with Change in anti-LY2605541 antibodies
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End point description:

The percentage of participants with a treatment-emergent anti-LY2605541 antibody response (TEAR) is summarized. TEAR is defined as change from baseline to post-baseline in the anti-LY2605541 antibody level either from undetectable to detectable or from detectable to the value with at least 130% relative increase from baseline.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable anti-LY2605541 antibody data at baseline and post-baseline. Missing endpoints were imputed with the LOCF method.

End point type	Secondary
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End point timeframe:

Baseline through 26 weeks and Baseline through 52 weeks and Baseline through 78 weeks

End point values	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288	153		
Units: percentage of participants				
number (not applicable)				
Week 26 (n=288, 152)	30.6	15.8		
Week 52 (n=288, 152)	29.9	17.1		
Week 78 (n=288, 153)	26.4	13.1		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Insulin Treatment Satisfaction Questionnaire (ITSQ)

End point title	Insulin Treatment Satisfaction Questionnaire (ITSQ)
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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 means were calculated using an analysis of covariance (ANCOVA) model with treatment and stratification (baseline HbA1c [ $\leq 8.5\%$  or  $> 8.5\%$ ] and country) as fixed effects and baseline value of the dependent variable as a covariate.

Participants who were randomized, had at least 1 dose of study medication, and had evaluable ITSQ data at both baseline and post-baseline. Missing endpoints were imputed with the LOCF method.

End point type	Secondary
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End point timeframe:

26 weeks

<b>End point values</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	273	149		
Units: units on a scale				
least squares mean (standard error)	72.43 (± 0.69)	73.91 (± 0.94)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: European Quality of Life-5 Dimension (EQ-5D)

End point title	European Quality of Life-5 Dimension (EQ-5D)
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End point description:

The EQ-5D is a generic, multidimensional, health-related, quality-of-life instrument. The profile allows participants to rate their health state in 5 health domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) using a 3-level scale of 1-3 (no problem, some problems, and extreme problems). These combinations of attributes are converted into a weighted health-state Index Score according to the United States population-based algorithm. Scores range from -0.11 to 1.0, where a score of 1.0 indicates perfect health. LS means were calculated using ANCOVA, adjusting for treatment and stratification factors (baseline HbA1c [ $\leq 8.5\%$  or  $> 8.5\%$ ] and country) as fixed effects and baseline EQ-5D score as a covariate.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable EQ-5D data at both baseline and post-baseline. Missing endpoints were imputed with the LOCF method.

End point type	Secondary
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End point timeframe:

26 weeks

<b>End point values</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	277	150		
Units: units on a scale				
least squares mean (standard error)	0.92 (± 0.01)	0.91 (± 0.01)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Low Blood Sugar Survey (LBSS)

End point title	Low Blood Sugar Survey (LBSS)
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End point description:

LBSS (also referenced as Hypoglycemia Fear Survey – II [HFS-II]) is a 33-item questionnaire that measures 1) behaviors to avoid hypoglycemia and its negative consequences (15 items) and 2) worries about hypoglycemia and its negative consequences (18 items). Responses are made on a 5-point Likert scale where 0 = Never and 4 = Always. Total score is the sum of all items (range 0-132). Higher total

scores reflect greater fear of hypoglycemia. LS means were calculated using MMRM, adjusting for treatment, stratification factors (baseline HbA1c [ $\leq 8.5\%$  and  $>8.5\%$ ] and country), visit, treatment-by-visit interaction, and corresponding baseline dependent variable as the fixed effects and participants as the random effect.

Analysis Population Description: Participants who were randomized, had at least 1 dose of study medication, and had evaluable LBSS data at both baseline and post-baseline.

End point type	Secondary
End point timeframe:	
26 weeks and 52 weeks and 78 weeks	

End point values	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	151		
Units: units on a scale				
least squares mean (standard error)				
Week 26	28.09 ( $\pm 0.7$ )	27.09 ( $\pm 0.95$ )		
Week 52	27.76 ( $\pm 0.77$ )	27 ( $\pm 1.01$ )		
Week 78	27.68 ( $\pm 0.91$ )	27.14 ( $\pm 1.18$ )		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Rapid Assessment of Physical Activity (RAPA)

End point title	Rapid Assessment of Physical Activity (RAPA)
End point description:	
<p>RAPA questionnaire assesses the level and intensity of physical activity of adult participants. It contains 2 subscales: RAPA 1 (Aerobic) and RAPA 2 (Strength and Flexibility). RAPA 1 contains 7 questions regarding the participant's amount and intensity of physical activity, allowing each participant's aerobic activity level to be categorized as sedentary, underactive, light activities, light activity, regular underactive, or active. RAPA 2 contains 2 questions regarding participants' physical activities that increase strength and improve flexibility. Each participant's strength and flexibility activity level is then categorized as neither strength nor flexibility (flex) activity, either strength or flex (not both), both strength and flex activity. The percentage of participants in each RAPA 1/2 category is presented and was calculated by dividing the number of participants in each RAPA 1/2 category by the total number of participants analyzed, then multiplying by 100.</p>	
End point type	Secondary
End point timeframe:	
26 weeks and 78 weeks	

<b>End point values</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98 <sup>[2]</sup>	57 <sup>[3]</sup>		
Units: percentage of participants				
number (not applicable)				
RAPA 1, Sedentary, Week 26 (n=98, 57)	1	0		
RAPA 1, Sedentary, Week 78 (n=80, 51)	1.3	0		
RAPA 1, Underactive, Week 26 (n=98, 57)	3.1	3.5		
RAPA 1, Underactive, Week 78 (n=80, 51)	3.8	2		
RAPA 1, Light activity, Week 26 (n=98, 57)	13.3	10.5		
RAPA 1, Light activity, Week 78 (n=80, 51)	7.5	13.7		
RAPA 1, Regular underactive, Week 26 (n=98, 57)	24.5	29.8		
RAPA 1, Regular underactive, Week 78 (n=80, 51)	31.3	29.4		
RAPA 1, Active, Week 26 (n=98, 57)	58.2	56.1		
RAPA 1, Active, Week 78 (n=80, 51)	56.3	54.9		
RAPA 2, Neither strength/flex, Week 26 (n=98, 57)	35.7	43.9		
RAPA 2, Neither strength/flex, Week 78 (n=81, 51)	37	47.1		
RAPA 2, Either strength/flex, Week 26 (n=98, 57)	30.6	35.1		
RAPA 2, Either strength/flex, Week 78 (n=81, 51)	33.3	29.4		
RAPA 2, Both strength/flex, Week 26 (n=98, 57)	33.7	21.1		
RAPA 2, Both strength/flex, Week 78 (n=81, 51)	29.6	23.5		

Notes:

[2] - Participants who were randomized, had at least 1 dose of study medication, & had evaluable RAPA data.

[3] - Missing endpoints were imputed with the LOCF method, using only post-baseline data.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Entire Study

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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### Reporting groups

Reporting group title	LY2605541 + Insulin Lispro
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Reporting group description: -

Reporting group title	Glargine + Insulin Lispro
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Reporting group description: -

<b>Serious adverse events</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro	
Total subjects affected by serious adverse events			
subjects affected / exposed	67 / 294 (22.79%)	25 / 159 (15.72%)	
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)			
Acute myeloid leukaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
basal cell carcinoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
benign bone neoplasm			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

breast cancer alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cervix carcinoma alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
fibroadenoma of breast alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
uterine leiomyoma alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Vascular disorders</b>			
intermittent claudication alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
peripheral arterial occlusive disease alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
peripheral artery stenosis alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Surgical and medical procedures</b>			
hysterectomy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
toe amputation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Immune system disorders</b>			
anaphylactic shock			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Reproductive system and breast disorders</b>			
cervical polyp			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
menorrhagia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ovarian cyst			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Respiratory, thoracic and mediastinal disorders</b>			
Acute respiratory distress syndrome alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary embolism alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary oedema alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Psychiatric disorders</b>			
Adjustment disorder alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
suicide attempt alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Injury, poisoning and procedural complications</b>			
Alcohol poisoning alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
clavicle fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
fall		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
incorrect dose administered		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
intentional overdose		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
lower limb fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
overdose		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0

road traffic accident alternative dictionary used: MedDRA 16.0 subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
tibia fracture alternative dictionary used: MedDRA 16.0 subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
atrial fibrillation alternative dictionary used: MedDRA 16.0 subjects affected / exposed	3 / 294 (1.02%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiomyopathy alternative dictionary used: MedDRA 16.0 subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
complicated migraine alternative dictionary used: MedDRA 16.0 subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dizziness alternative dictionary used: MedDRA 16.0 subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoglycaemic coma alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Ear and labyrinth disorders</b>			
sudden hearing loss			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
tympanic membrane perforation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Gastrointestinal disorders</b>			
faeces pale			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
impaired gastric emptying			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancreatitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancreatitis acute			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
small intestinal perforation alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders hepatic function abnormal alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders skin ulcer alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders renal failure acute alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary incontinence alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders intervertebral disc degeneration alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
intervertebral disc protrusion alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lumbar spinal stenosis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
muscle contracture alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
spondylolisthesis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
Abscess limb alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cellulitis alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
chronic sinusitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
diabetic gangrene		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
gastroenteritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
infectious mononucleosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
osteomyelitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
pneumonia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0

pneumonia bacterial alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
post procedural sepsis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pseudomonas infection alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
sepsis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
staphylococcal sepsis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
diabetic ketoacidosis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoglycaemia alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	45 / 294 (15.31%)	13 / 159 (8.18%)
occurrences causally related to treatment / all	61 / 73	17 / 20
deaths causally related to treatment / all	0 / 0	0 / 0
hyponatraemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
ketoacidosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
metabolic disorder		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

<b>Non-serious adverse events</b>	LY2605541 + Insulin Lispro	Glargine + Insulin Lispro
Total subjects affected by non-serious adverse events		
subjects affected / exposed	256 / 294 (87.07%)	112 / 159 (70.44%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
angiomyolipoma		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
eye naevus		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0

<p>haemangioma of liver</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 294 (0.68%)</p> <p>2</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	
<p>lipoma</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 294 (0.68%)</p> <p>2</p>	<p>1 / 159 (0.63%)</p> <p>1</p>	
<p>thyroid neoplasm</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 294 (0.00%)</p> <p>0</p>	<p>1 / 159 (0.63%)</p> <p>1</p>	
<p>uterine leiomyoma</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 294 (0.34%)</p> <p>1</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	
<p>Vascular disorders</p> <p>aortic arteriosclerosis</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 294 (0.34%)</p> <p>1</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	
<p>deep vein thrombosis</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 294 (0.68%)</p> <p>2</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	
<p>haematoma</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 294 (0.68%)</p> <p>2</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	
<p>hyperaemia</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 294 (0.68%)</p> <p>3</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	
<p>hypertension</p> <p>alternative dictionary used: MedDRA 16.0</p>			

subjects affected / exposed	10 / 294 (3.40%)	1 / 159 (0.63%)	
occurrences (all)	10	1	
hypotension			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)	
occurrences (all)	1	1	
phlebitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences (all)	1	0	
thrombophlebitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences (all)	0	1	
varicose vein			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences (all)	1	0	
venous thrombosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences (all)	1	0	
vessel perforation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			
abortion induced			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences (all)	1	0	
blepharoplasty			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
cardiac ablation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
cataract operation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
Colon polypectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
cyst removal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
dental care		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
dental implantation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
diabetes mellitus management		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
endodontic procedure		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0

face lift		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
hysterectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
inguinal hernia repair		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
liposuction		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
mass excision		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
mole excision		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
oral surgery		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
retinal laser coagulation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	4	0
tendon sheath incision		
alternative dictionary used: MedDRA 16.0		

<p>subjects affected / exposed occurrences (all)</p> <p>thrombosis prophylaxis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>toe operation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>tooth extraction alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>tumour excision alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p>	<p>1 / 294 (0.34%) 1</p> <p>1 / 294 (0.34%) 1</p> <p>1 / 294 (0.34%) 1</p> <p>4 / 294 (1.36%) 4</p> <p>1 / 294 (0.34%) 1</p>	<p>2 / 159 (1.26%) 3</p> <p>0 / 159 (0.00%) 0</p> <p>0 / 159 (0.00%) 0</p> <p>4 / 159 (2.52%) 4</p> <p>0 / 159 (0.00%) 0</p>	
<p>Pregnancy, puerperium and perinatal conditions pregnancy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p>	<p>1 / 294 (0.34%) 1</p>	<p>2 / 159 (1.26%) 2</p>	
<p>General disorders and administration site conditions asthenia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>chest pain alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>chills alternative dictionary used: MedDRA 16.0</p>	<p>1 / 294 (0.34%) 1</p> <p>4 / 294 (1.36%) 4</p>	<p>1 / 159 (0.63%) 1</p> <p>0 / 159 (0.00%) 0</p>	

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
drug intolerance		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
fat tissue increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
fatigue		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	6 / 294 (2.04%)	2 / 159 (1.26%)
occurrences (all)	6	2
feeling cold		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
hernia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
induration		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
inflammation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
influenza like illness		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0

infusion site extravasation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0
injection site atrophy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 294 (0.68%) 5	0 / 159 (0.00%) 0
injection site bruising alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	1 / 159 (0.63%) 1
injection site discomfort alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 2	0 / 159 (0.00%) 0
injection site haematoma alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	1 / 159 (0.63%) 2
injection site hypertrophy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	8 / 294 (2.72%) 9	0 / 159 (0.00%) 0
injection site mass alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0
injection site oedema alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	5 / 294 (1.70%) 5	0 / 159 (0.00%) 0
injection site pain alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
injection site pruritus		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
injection site reaction		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 294 (1.36%)	0 / 159 (0.00%)
occurrences (all)	6	0
injection site swelling		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 294 (1.36%)	0 / 159 (0.00%)
occurrences (all)	7	0
instillation site reaction		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
local swelling		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
malaise		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
oedema peripheral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 294 (1.36%)	0 / 159 (0.00%)
occurrences (all)	5	0
pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0

<p>pyrexia</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>8 / 294 (2.72%)</p> <p>8</p>	<p>3 / 159 (1.89%)</p> <p>3</p>	
<p>vessel puncture site pain</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 294 (0.00%)</p> <p>0</p>	<p>1 / 159 (0.63%)</p> <p>1</p>	
<p>Immune system disorders</p> <p>allergy to animal</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>allergy to arthropod bite</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>house dust allergy</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>seasonal allergy</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 294 (0.34%)</p> <p>1</p> <p>1 / 294 (0.34%)</p> <p>1</p> <p>1 / 294 (0.34%)</p> <p>1</p> <p>3 / 294 (1.02%)</p> <p>3</p>	<p>0 / 159 (0.00%)</p> <p>0</p> <p>0 / 159 (0.00%)</p> <p>0</p> <p>0 / 159 (0.00%)</p> <p>2 / 159 (1.26%)</p> <p>3</p>	
<p>Social circumstances</p> <p>menopause</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>tobacco user</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 294 (0.34%)</p> <p>1</p> <p>1 / 294 (0.34%)</p> <p>1</p>	<p>1 / 159 (0.63%)</p> <p>1</p> <p>0 / 159 (0.00%)</p> <p>0</p>	
<p>Reproductive system and breast disorders</p>			

amenorrhoea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
breast mass		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
dysmenorrhoea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	3 / 159 (1.89%)
occurrences (all)	6	4
fibrocystic breast disease		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
menstruation irregular		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
ovarian cyst		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
pelvic pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
polymenorrhoea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
pruritus genital		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
testicular pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
<b>Respiratory, thoracic and mediastinal disorders</b>		
acute lung injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
asthma		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
bronchitis chronic		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
cough		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	9 / 294 (3.06%)	5 / 159 (3.14%)
occurrences (all)	12	6
dysphonia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
epistaxis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
haemoptysis		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
nasal congestion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	1 / 159 (0.63%)
occurrences (all)	2	1
nasal inflammation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
oropharyngeal pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	7 / 294 (2.38%)	4 / 159 (2.52%)
occurrences (all)	7	4
pleural effusion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
respiratory tract congestion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
rhinitis allergic		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	1 / 159 (0.63%)
occurrences (all)	3	1
sinus congestion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
sleep apnoea syndrome		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0

sneezing alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
throat irritation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
upper respiratory tract inflammation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	2 / 159 (1.26%) 3	
Psychiatric disorders			
alcohol abuse alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
anxiety alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	3 / 294 (1.02%) 3	0 / 159 (0.00%) 0	
depression alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 294 (0.68%) 2	5 / 159 (3.14%) 5	
drug dependence alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
emotional disorder alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
insomnia alternative dictionary used: MedDRA 16.0			

subjects affected / exposed occurrences (all)	3 / 294 (1.02%) 4	2 / 159 (1.26%) 2	
mental disorder alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
mood altered alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
suicidal ideation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
Hepatobiliary disorders Cholelithiasis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
gallbladder polyp alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
hepatic steatosis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	4 / 294 (1.36%) 4	1 / 159 (0.63%) 1	
Investigations alanine aminotransferase increased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	12 / 294 (4.08%) 20	1 / 159 (0.63%) 1	
aspartate aminotransferase increased alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	8 / 294 (2.72%)	1 / 159 (0.63%)
occurrences (all)	10	1
bacterial test positive		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
biopsy breast		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
blood alkaline phosphatase increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
blood bicarbonate decreased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
blood bilirubin increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)
occurrences (all)	1	1
blood creatine phosphokinase increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 294 (1.36%)	1 / 159 (0.63%)
occurrences (all)	4	1
blood triglycerides increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 294 (1.36%)	0 / 159 (0.00%)
occurrences (all)	5	0
electrocardiogram repolarisation abnormality		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
helicobacter test positive alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
hepatic enzyme increased alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	6 / 294 (2.04%) 6	1 / 159 (0.63%) 1	
liver function test abnormal alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	4 / 294 (1.36%) 4	0 / 159 (0.00%) 0	
transaminases increased alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
weight decreased alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	6 / 294 (2.04%) 6	1 / 159 (0.63%) 1	
weight increased alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	4 / 294 (1.36%) 4	6 / 159 (3.77%) 6	
Injury, poisoning and procedural complications animal bite alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
ankle fracture alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
arthropod bite		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)
occurrences (all)	1	1
avulsion fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
chillblains		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
contusion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	1 / 159 (0.63%)
occurrences (all)	3	1
corneal abrasion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
epicondylitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	2	0
excoriation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	1 / 159 (0.63%)
occurrences (all)	2	1
fall		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	0 / 159 (0.00%)
occurrences (all)	3	0

foot fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	3 / 159 (1.89%)
occurrences (all)	3	3
fracture displacement		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
gastrointestinal disorder postoperative		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
hand fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)
occurrences (all)	1	1
head injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
intentional overdose		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	3	0
joint dislocation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
joint injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
laceration		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	2 / 294 (0.68%)	1 / 159 (0.63%)
occurrences (all)	2	1
ligament sprain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 294 (1.70%)	2 / 159 (1.26%)
occurrences (all)	5	2
limb injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
meniscus injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
muscle contusion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
muscle injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
muscle rupture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
muscle strain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
nail injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0

overdose		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)
occurrences (all)	2	1
patella fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
post procedural complication		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)
occurrences (all)	1	1
procedural nausea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
procedural pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
rib fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	2 / 159 (1.26%)
occurrences (all)	1	2
road traffic accident		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
tendon rupture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
tibia fracture		
alternative dictionary used: MedDRA 16.0		

<p>subjects affected / exposed occurrences (all)</p> <p>tooth fracture alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>traumatic ulcer alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>wound alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>wrist fracture alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>wrong drug administered alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p>	<p>1 / 294 (0.34%) 1</p> <p>0 / 294 (0.00%) 0</p> <p>1 / 294 (0.34%) 1</p> <p>3 / 294 (1.02%) 3</p> <p>1 / 294 (0.34%) 1</p> <p>2 / 294 (0.68%) 2</p>	<p>0 / 159 (0.00%) 0</p> <p>1 / 159 (0.63%) 1</p> <p>0 / 159 (0.00%) 0</p> <p>0 / 159 (0.00%) 0</p> <p>0 / 159 (0.00%) 0</p> <p>0 / 159 (0.00%) 0</p>	
<p>Congenital, familial and genetic disorders phimosis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p>	<p>0 / 294 (0.00%) 0</p>	<p>1 / 159 (0.63%) 1</p>	
<p>Cardiac disorders angina pectoris alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>arteriosclerosis coronary artery alternative dictionary used: MedDRA 16.0</p>	<p>1 / 294 (0.34%) 1</p>	<p>0 / 159 (0.00%) 0</p>	

subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
left ventricular hypertrophy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
palpitations alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	3 / 294 (1.02%) 3	0 / 159 (0.00%) 0	
sick sinus syndrome alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
sinus tachycardia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
tachycardia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
ventricular extrasystoles alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	1 / 159 (0.63%) 1	
Nervous system disorders carpal tunnel syndrome alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
cervicobrachial syndrome alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
diabetic neuropathy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	1 / 159 (0.63%)
occurrences (all)	3	1
dizziness		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 294 (1.70%)	4 / 159 (2.52%)
occurrences (all)	6	4
headache		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	18 / 294 (6.12%)	10 / 159 (6.29%)
occurrences (all)	27	13
hypertonia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
hypoesthesia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
hypokinesia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
migraine		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
nerve compression		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1

paraesthesia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 294 (0.68%) 2	0 / 159 (0.00%) 0	
restless legs syndrome alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
sciatica alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
sinus headache alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
somnolence alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
tension headache alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
<b>Blood and lymphatic system disorders</b>			
anaemia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	3 / 294 (1.02%) 3	2 / 159 (1.26%) 2	
iron deficiency anaemia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 294 (0.68%) 2	0 / 159 (0.00%) 0	
lymphadenitis alternative dictionary used: MedDRA 16.0			

<p>subjects affected / exposed occurrences (all)</p> <p>lymphadenopathy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>microcytic anaemia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>pancytopenia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p>	<p>1 / 294 (0.34%) 1</p> <p>1 / 294 (0.34%) 1</p> <p>1 / 294 (0.34%) 1</p> <p>0 / 294 (0.00%) 0</p>	<p>0 / 159 (0.00%) 0</p> <p>0 / 159 (0.00%) 0</p> <p>0 / 159 (0.00%) 0</p> <p>1 / 159 (0.63%) 1</p>	
<p>Ear and labyrinth disorders tinnitus alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>vertigo positional alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p>	<p>2 / 294 (0.68%) 2</p> <p>1 / 294 (0.34%) 1</p>	<p>0 / 159 (0.00%) 0</p> <p>0 / 159 (0.00%) 0</p>	
<p>Eye disorders cataract alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>conjunctivitis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)</p> <p>conjunctivitis allergic alternative dictionary used: MedDRA 16.0</p>	<p>3 / 294 (1.02%) 3</p> <p>5 / 294 (1.70%) 5</p>	<p>0 / 159 (0.00%) 0</p> <p>2 / 159 (1.26%) 2</p>	

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
diabetic retinal oedema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	2	0
diabetic retinopathy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	7 / 294 (2.38%)	0 / 159 (0.00%)
occurrences (all)	8	0
dry eye		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
eye haemorrhage		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
eye pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	1 / 159 (0.63%)
occurrences (all)	2	1
keratitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
macular degeneration		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
macular oedema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0

<p>pingueculitis</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 294 (0.00%)</p> <p>0</p>	<p>1 / 159 (0.63%)</p> <p>1</p>	
<p>retinal aneurysm</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 294 (0.00%)</p> <p>0</p>	<p>1 / 159 (0.63%)</p> <p>1</p>	
<p>retinopathy</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 294 (1.02%)</p> <p>3</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	
<p>vision blurred</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 294 (0.34%)</p> <p>1</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	
<p>visual acuity reduced</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 294 (0.34%)</p> <p>1</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	
<p>vitreous haemorrhage</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 294 (0.34%)</p> <p>1</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	
<p>Gastrointestinal disorders</p> <p>abdominal discomfort</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 294 (0.34%)</p> <p>1</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	
<p>abdominal distension</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 294 (1.02%)</p> <p>3</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	
<p>abdominal pain</p> <p>alternative dictionary used: MedDRA 16.0</p>			

subjects affected / exposed	5 / 294 (1.70%)	1 / 159 (0.63%)
occurrences (all)	5	2
abdominal pain lower		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)
occurrences (all)	1	1
abdominal pain upper		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 294 (1.36%)	3 / 159 (1.89%)
occurrences (all)	5	3
anal polyp		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
Coeliac disease		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
constipation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	1 / 159 (0.63%)
occurrences (all)	3	1
dental caries		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
diarrhoea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	13 / 294 (4.42%)	3 / 159 (1.89%)
occurrences (all)	15	3
dyspepsia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 294 (1.36%)	0 / 159 (0.00%)
occurrences (all)	4	0

enteritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
flatulence		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
food poisoning		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 294 (1.36%)	4 / 159 (2.52%)
occurrences (all)	4	4
gastric mucosa erythema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	3	0
gastric ulcer		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
gastritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	7 / 294 (2.38%)	3 / 159 (1.89%)
occurrences (all)	8	3
gastritis erosive		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
gastrooesophageal reflux disease		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	6 / 294 (2.04%)	1 / 159 (0.63%)
occurrences (all)	7	1
haematochezia		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
haemorrhoids		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	2
melanosis coli		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
nausea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	8 / 294 (2.72%)	4 / 159 (2.52%)
occurrences (all)	9	4
pancreatic insufficiency		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
paraesthesia oral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	2	0
stomatitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
tooth disorder		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
tooth loss		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0

toothache alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	4 / 294 (1.36%) 4	1 / 159 (0.63%) 1	
umbilical hernia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
vomiting alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	7 / 294 (2.38%) 9	3 / 159 (1.89%) 3	
<b>Skin and subcutaneous tissue disorders</b>			
acne alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
alopecia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 294 (0.68%) 2	0 / 159 (0.00%) 0	
blister alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
dermal cyst alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
dermatitis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
dermatitis allergic alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
dermatitis contact		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	3	0
eczema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	2 / 159 (1.26%)
occurrences (all)	3	2
erythema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
haemorrhage subcutaneous		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
hyperhidrosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
hyperkeratosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
ingrowing nail		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
lipodystrophy acquired		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	17 / 294 (5.78%)	1 / 159 (0.63%)
occurrences (all)	24	1

lipohypertrophy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	45 / 294 (15.31%)	0 / 159 (0.00%)
occurrences (all)	66	0
neurodermatitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
night sweats		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
panniculitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
petechiae		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
pruritus		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	1 / 159 (0.63%)
occurrences (all)	3	1
skin mass		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
skin ulcer		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	2 / 159 (1.26%)
occurrences (all)	2	3
swelling face		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
urticaria		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	3 / 159 (1.89%)
occurrences (all)	4	3
urticaria chronic		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
<b>Renal and urinary disorders</b>		
albuminuria		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)
occurrences (all)	1	2
cystitis noninfective		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
dysuria		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
microalbuminuria		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 294 (1.36%)	0 / 159 (0.00%)
occurrences (all)	4	0
nephrolithiasis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	1 / 159 (0.63%)
occurrences (all)	2	1
neurogenic bladder		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
polyuria alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
renal cyst alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
urinary incontinence alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
urinary retention alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
Endocrine disorders			
autoimmune thyroiditis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
basedow's disease alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
goitre alternative dictionary used: MedDRA 16.0			
subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
thyroiditis alternative dictionary used: MedDRA 16.0			

subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
arthralgia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 294 (0.68%) 2	4 / 159 (2.52%) 4	
back pain alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	15 / 294 (5.10%) 17	7 / 159 (4.40%) 7	
bone formation increased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
bursitis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
exostosis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
groin pain alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
hypercreatinaemia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
intervertebral disc disorder alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
intervertebral disc protrusion alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 294 (1.70%)	0 / 159 (0.00%)
occurrences (all)	5	0
joint swelling alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
muscle atrophy alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
muscle spasms alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
muscular weakness alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
musculoskeletal chest pain alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
musculoskeletal pain alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	0 / 159 (0.00%)
occurrences (all)	3	0
myalgia alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	3 / 159 (1.89%)
occurrences (all)	1	3

myositis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
neck pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
pain in extremity		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	7 / 294 (2.38%)	3 / 159 (1.89%)
occurrences (all)	8	3
periarthritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
polyarthritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
rotator cuff syndrome		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
spondylolisthesis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
tendon pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
tendonitis		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed occurrences (all)	2 / 294 (0.68%) 2	1 / 159 (0.63%) 1	
trigger finger alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	1 / 159 (0.63%) 1	
<b>Infections and infestations</b>			
acarodermatitis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
acute sinusitis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 294 (0.68%) 2	0 / 159 (0.00%) 0	
acute tonsillitis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 2	0 / 159 (0.00%) 0	
anal abscess alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 294 (0.34%) 1	0 / 159 (0.00%) 0	
bacterial infection alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 294 (0.00%) 0	1 / 159 (0.63%) 1	
bacterial rhinitis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 294 (0.68%) 2	0 / 159 (0.00%) 0	
bronchitis alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	11 / 294 (3.74%)	4 / 159 (2.52%)
occurrences (all)	12	4
cellulitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	2 / 159 (1.26%)
occurrences (all)	0	4
conjunctivitis bacterial		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
cystitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	9 / 294 (3.06%)	3 / 159 (1.89%)
occurrences (all)	10	3
ear infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	0 / 159 (0.00%)
occurrences (all)	3	0
enterobiasis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
eye infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
fungal infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	1 / 159 (0.63%)
occurrences (all)	2	1
gastroenteritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	11 / 294 (3.74%)	8 / 159 (5.03%)
occurrences (all)	11	9

gastroenteritis bacterial		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
gastroenteritis viral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 294 (1.36%)	5 / 159 (3.14%)
occurrences (all)	4	6
gastrointestinal infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	0 / 159 (0.00%)
occurrences (all)	5	0
genital infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
gingivitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)
occurrences (all)	1	1
hand-foot-and-mouth disease		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
helicobacter gastritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
herpes virus infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
herpes zoster		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	3 / 294 (1.02%)	0 / 159 (0.00%)
occurrences (all)	3	0
hordeolum		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	2 / 159 (1.26%)
occurrences (all)	1	2
influenza		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	25 / 294 (8.50%)	14 / 159 (8.81%)
occurrences (all)	32	14
laryngitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
lice infestation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
localised infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
mastitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
nail infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
nasopharyngitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	92 / 294 (31.29%)	38 / 159 (23.90%)
occurrences (all)	152	61

onychomycosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	2	0
oral fungal infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
oral herpes		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	1 / 159 (0.63%)
occurrences (all)	2	1
otitis externa		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)
occurrences (all)	1	1
otitis media		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	2 / 159 (1.26%)
occurrences (all)	2	2
papilloma viral infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
periodontitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
pharyngitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	13 / 294 (4.42%)	7 / 159 (4.40%)
occurrences (all)	19	9
pharyngitis bacterial		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	3 / 294 (1.02%)	1 / 159 (0.63%)
occurrences (all)	3	4
pharyngitis streptococcal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	2 / 159 (1.26%)
occurrences (all)	3	2
pneumonia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)
occurrences (all)	1	1
pulpitis dental		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	1 / 159 (0.63%)
occurrences (all)	5	1
purulence		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
respiratory tract infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	0 / 159 (0.00%)
occurrences (all)	3	0
respiratory tract infection viral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
rhinitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 294 (1.36%)	0 / 159 (0.00%)
occurrences (all)	4	0
sinusitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	7 / 294 (2.38%)	4 / 159 (2.52%)
occurrences (all)	8	5

staphylococcal infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
staphylococcal osteomyelitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
tinea infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
tinea pedis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
tooth abscess		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	3 / 159 (1.89%)
occurrences (all)	1	4
tooth infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
tracheitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	2 / 159 (1.26%)
occurrences (all)	1	2
tracheobronchitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
upper respiratory tract infection		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	13 / 294 (4.42%)	12 / 159 (7.55%)	
occurrences (all)	22	17	
urinary tract infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	15 / 294 (5.10%)	8 / 159 (5.03%)	
occurrences (all)	17	14	
vaginal infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences (all)	1	0	
viral infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)	
occurrences (all)	1	1	
viral rash			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences (all)	0	1	
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences (all)	1	0	
vulvovaginal mycotic infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	1 / 159 (0.63%)	
occurrences (all)	1	1	
wound infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
central obesity			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
decreased appetite		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 294 (1.70%)	0 / 159 (0.00%)
occurrences (all)	5	0
dehydration		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
dyslipidaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	2 / 159 (1.26%)
occurrences (all)	3	2
electrolyte imbalance		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 294 (0.00%)	1 / 159 (0.63%)
occurrences (all)	0	1
fluid retention		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 294 (0.68%)	1 / 159 (0.63%)
occurrences (all)	3	1
hyperalbuminaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)
occurrences (all)	1	0
hypercholesterolaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 294 (1.36%)	2 / 159 (1.26%)
occurrences (all)	4	2
hyperglycaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 294 (1.02%)	0 / 159 (0.00%)
occurrences (all)	3	0

hyperlipidaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 294 (1.02%)	0 / 159 (0.00%)	
occurrences (all)	3	0	
hypertriglyceridaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences (all)	1	0	
hyperuricaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences (all)	1	0	
iron deficiency			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	0 / 159 (0.00%)	
occurrences (all)	2	0	
vitamin d deficiency			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 294 (0.34%)	2 / 159 (1.26%)	
occurrences (all)	1	2	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 September 2011	Secondary objective related to safety measures was added. Discontinuation criteria was revised. Statistical analysis plan was updated. Information for the blood glucose meter was added.
07 September 2012	Added additional information to clarify insulin dosing plans. Statistical Analysis plan was updated.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported