



Clinical trial results:

A Comparison of LY2605541 versus Insulin Glargine Alone or in Combination with Pre-study Oral Antihyperglycemic Medications in Patients with Type 2 Diabetes Mellitus Previously Treated with Basal Insulin: An Open-Label, Randomized Study The IMAGINE 5 Study

Summary

EudraCT number	2011-005866-39
Trial protocol	ES DE GR CZ
Global end of trial date	17 December 2013

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-BIDJ
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01582451
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 14703

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, 1 877-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559,

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	17 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 December 2013
Global end of trial reached?	Yes
Global end of trial date	17 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to compare LY2605541 and insulin glargine using the following measures after participants have been treated for 26 weeks:

- Change in participants' overall blood sugar control
- The rate of night time low blood sugar episodes
- The number of participants that reach blood sugar targets without low blood sugar episodes at night
- The rate of low blood sugar episodes reported over a 24-hour period

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	23 April 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	United States: 255
Country: Number of subjects enrolled	Czech Republic: 30
Country: Number of subjects enrolled	Greece: 21
Country: Number of subjects enrolled	Spain: 39
Country: Number of subjects enrolled	Romania: 30
Country: Number of subjects enrolled	Israel: 24
Country: Number of subjects enrolled	Russian Federation: 26
Country: Number of subjects enrolled	Germany: 41
Worldwide total number of subjects	466
EEA total number of subjects	161

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	295
From 65 to 84 years	169
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

No text entered.

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
Arm title	Insulin Peglispro (LY2605541)

Arm description:

Insulin peglispro (LY2605541) was administered by subcutaneous (SQ) injection once daily at bedtime for up to 52 weeks. Initial dose based on dose of prestudy basal insulin and adjusted based on fasting blood glucose (FBG).

Arm type	Experimental
Investigational medicinal product name	Insulin peglispro
Investigational medicinal product code	
Other name	LY2605541
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous (SQ) injection once daily at bedtime. Initial dose based on dose of prestudy basal insulin and adjusted based on fasting blood glucose (FBG). LY2605541 will be given alone or in combination with up to 3 pre-study oral antihyperglycemic medications (OAMs) whose use is not excluded in combination with insulin.

Arm title	Insulin glargine
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Arm description:

Insulin glargine was administered by SQ injection once daily at bedtime for up to 52 weeks. Initial dose based on dose of prestudy basal insulin and adjusted based on FBG.

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

Dosage and administration details:

Administered by SQ injection once daily at bedtime. Initial dose based on dose of prestudy basal insulin and adjusted based on FBG. Insulin glargine will be used alone or in combination with up to 3 pre-study OAMs whose use is not excluded in combination with insulin.

Number of subjects in period 1	Insulin Peglispro (LY2605541)	Insulin glargine
Started	307	159
Received at least 1 dose of study drug	305	159
Completed	275	139
Not completed	32	20
Adverse event, serious fatal	3	3
Consent withdrawn by subject	13	9
Physician decision	3	-
Adverse event, non-fatal	1	3
Sponsor Decision	1	-
Lost to follow-up	-	2
Protocol deviation	11	3

Baseline characteristics

Reporting groups

Reporting group title	Insulin Peglispro (LY2605541)
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Reporting group description:

Insulin peglispro (LY2605541) was administered by subcutaneous (SQ) injection once daily at bedtime for up to 52 weeks. Initial dose based on dose of prestudy basal insulin and adjusted based on fasting blood glucose (FBG).

Reporting group title	Insulin glargine
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Reporting group description:

Insulin glargine was administered by SQ injection once daily at bedtime for up to 52 weeks. Initial dose based on dose of prestudy basal insulin and adjusted based on FBG.

Reporting group values	Insulin Peglispro (LY2605541)	Insulin glargine	Total
Number of subjects	307	159	466
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	307	157	464
85 years and over	0	2	2
Age Continuous Units: years			
arithmetic mean	61.84	60.38	-
standard deviation	± 8.52	± 10.10	-
Gender, Male/Female Units: Participants			
Female	132	66	198
Male	175	93	268
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	57	25	82
Not Hispanic or Latino	215	115	330
Unknown or Not Reported	35	19	54
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	0	2
Asian	4	2	6
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	17	9	26
White	280	148	428
More than one race	1	0	1

Unknown or Not Reported	2	0	2
Region of Enrollment			
Units: Subjects			
United States	170	85	255
Czech Republic	20	10	30
Greece	16	5	21
Spain	27	12	39
Romania	16	14	30
Israel	16	8	24
Russian Federation	17	9	26
Germany	25	16	41

End points

End points reporting groups

Reporting group title	Insulin Peglispro (LY2605541)
Reporting group description: Insulin peglispro (LY2605541) was administered by subcutaneous (SQ) injection once daily at bedtime for up to 52 weeks. Initial dose based on dose of prestudy basal insulin and adjusted based on fasting blood glucose (FBG).	
Reporting group title	Insulin glargine
Reporting group description: Insulin glargine was administered by SQ injection once daily at bedtime for up to 52 weeks. Initial dose based on dose of prestudy basal insulin and adjusted based on FBG.	

Primary: Change from baseline to 26-week endpoint in hemoglobin A1c (HbA1c)

End point title	Change from baseline to 26-week endpoint in hemoglobin A1c (HbA1c)
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 stratification factors (country, baseline low-density lipoprotein cholesterol [LDL-C, <100 milligrams per deciliter (mg/dL) and ≥100 mg/dL], and sulfonylurea (SU) or meglitinide use), visit, treatment, visit-by-treatment interaction, and baseline HbA1c.	
End point type	Primary
End point timeframe: Baseline, 26 weeks	

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302 ^[1]	157 ^[2]		
Units: percentage of HbA1c				
least squares mean (standard error)	-0.82 (± 0.04)	-0.29 (± 0.06)		

Notes:

[1] - Participants who were randomized, had at least 1 dose of study drug and evaluable data.

[2] - Participants who were randomized, had at least 1 dose of study drug and evaluable data.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: MMRM approach that adjusts for missing data through a variance-covariance structure.	
Comparison groups	Insulin Peglispro (LY2605541) v Insulin glargine

Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA

Secondary: Change from baseline to 52 weeks in HbA1c

End point title	Change from baseline to 52 weeks in HbA1c
End point description: LS means were calculated using MMRM adjusting for stratification factors (country, baseline LDL-C [<100 mg/dL and ≥ 100 mg/dL], and SU or meglitinide use), visit, treatment, visit-by-treatment interaction, and baseline HbA1c.	
End point type	Secondary
End point timeframe: Baseline, 52 weeks	

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302 ^[3]	157 ^[4]		
Units: percentage of HbA1c				
least squares mean (standard error)	-0.67 (\pm 0.05)	-0.22 (\pm 0.06)		

Notes:

[3] - Participants who were randomized, had at least 1 dose of study drug and evaluable data.

[4] - Participants who were randomized, had at least 1 dose of study drug and evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of total and nocturnal hypoglycemia events (adjusted by 30 days)

End point title	Rate of total and nocturnal hypoglycemia events (adjusted by 30 days)
End point description: Hypoglycemic episodes are defined as events which are associated with reported signs and symptoms of hypoglycemia and/or documented blood glucose (BG) concentrations of ≤ 70 mg/dL (3.9 millimoles per liter [mmol/L]). A nocturnal hypoglycemic event occurred between bedtime and waking. Group mean rates of total and nocturnal hypoglycemia (per 30 days) are presented and were calculated from negative binomial regression models (number of episodes = treatment + baseline hypoglycemia rate + baseline SU or meglitinide use, 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.	
End point type	Secondary
End point timeframe: Baseline through 26 weeks and Baseline through 52 weeks	

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304 ^[5]	159 ^[6]		
Units: events/participant/30 days				
least squares mean (standard error)				
Total hypoglycemia, 0-26 weeks	1.55 (± 0.13)	1.98 (± 0.19)		
Total hypoglycemia, 0-52 weeks	1.24 (± 0.10)	1.62 (± 0.15)		
Nocturnal hypoglycemia, 0-26 weeks	0.43 (± 0.06)	1.04 (± 0.15)		
Nocturnal hypoglycemia, 0-52 weeks	0.35 (± 0.06)	0.88 (± 0.14)		

Notes:

[5] - Participants who were randomized, had at least 1 dose of study drug and evaluable data.

[6] - Participants who were randomized, had at least 1 dose of study drug and evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants that have total and nocturnal hypoglycemic events

End point title	Percentage of participants that have total and nocturnal hypoglycemic events
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End point description:

Hypoglycemic episodes are defined as events which are associated with reported signs and symptoms of hypoglycemia and/or documented BG concentrations of ≤ 70 mg/dL (3.9 mmol/L). A nocturnal hypoglycemic event occurred between bedtime and waking. The percentage of participants was calculated by dividing the number of participants with hypoglycemic episodes by the total number of participants analyzed, multiplied by 100.

End point type	Secondary
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End point timeframe:

Baseline through 26 weeks and Baseline through 52 weeks

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304 ^[7]	159 ^[8]		
Units: percentage of participants				
number (not applicable)				
Total hypoglycemia, 0-26 weeks	76.3	80.5		
Total hypoglycemia, 0-52 weeks	80.3	83.0		
Nocturnal hypoglycemia, 0-26 weeks	46.1	62.3		
Nocturnal hypoglycemia, 0-52 weeks	50.3	67.3		

Notes:

[7] - Participants who were randomized, had at least 1 dose of study medication, and had evaluable data.

[8] - Participants who were randomized, had at least 1 dose of study medication, and had evaluable data.

Statistical analyses

Secondary: Percentage of participants with HbA1c equal to or less than (\leq) 6.5% and less than ($<$) 7.0%

End point title	Percentage of participants with HbA1c equal to or less than (\leq) 6.5% and less than ($<$) 7.0%
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End point description:

The percentage of participants was calculated by dividing the number of participants reaching target HbA1c by the total number of participants analyzed, multiplied by 100.

End point type	Secondary
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End point timeframe:

26 and 52 weeks

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302 ^[9]	157 ^[10]		
Units: percentage of participants				
number (not applicable)				
HbA1c \leq 6.5%, 26 weeks	50.3	28.7		
HbA1c \leq 6.5%, 52 weeks	43.4	28.0		
HbA1c $<$ 7.0%, 26 weeks	72.5	52.2		
HbA1c $<$ 7.0%, 52 weeks	63.9	45.9		

Notes:

[9] - All randomized participants who had 1 dose of study drug and evaluable HbA1c data.

[10] - All randomized participants who had 1 dose of study drug and evaluable HbA1c data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HbA1c $<$ 7.0% and without nocturnal hypoglycemia

End point title	Percentage of participants with HbA1c $<$ 7.0% and without nocturnal hypoglycemia
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End point description:

Hypoglycemic episodes are defined as an event which is associated with reported signs and symptoms of hypoglycemia and/or a documented blood glucose concentration of \leq 70 mg/dL (3.9 mmol/L). A nocturnal hypoglycemic event occurred between bedtime and waking. 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, multiplied by 100.

End point type	Secondary
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End point timeframe:

26 and 52 weeks

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302 ^[11]	157 ^[12]		
Units: percentage of participants				
number (not applicable)				
26 weeks	40.1	18.5		
52 weeks	34.8	10.2		

Notes:

[11] - Randomized participants who had 1 dose of study drug and evaluable Hb1ac data.

[12] - All randomized participants who had 1 dose of study drug and evaluable HbA1c data.

Statistical analyses

No statistical analyses for this end point

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

End point title	Fasting serum glucose (FSG) (by laboratory)
End point description:	
LS means were calculated using MMRM adjusting for stratification factors (country, baseline HbA1c [$\leq 8.0\%$ and $> 8.0\%$], baseline LDL-C [< 100 mg/dL and ≥ 100 mg/dL], and SU or meglitinide use), visit, treatment, visit-by-treatment interaction, and baseline FSG.	
End point type	Secondary
End point timeframe:	
26 and 52 weeks	

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302 ^[13]	157 ^[14]		
Units: milligrams per deciliter (mg/dL)				
least squares mean (standard error)				
26 weeks	103.80 (\pm 1.88)	119.50 (\pm 2.64)		
52 weeks	107.61 (\pm 1.94)	115.74 (\pm 2.72)		

Notes:

[13] - Randomized participants who had at least 1 dose of study drug and evaluable FSG data.

[14] - Randomized participants who had at least 1 dose of study drug and evaluable FSG data.

Statistical analyses

No statistical analyses for this end point

Secondary: Fasting blood glucose (FBG) (by self monitoring)

End point title	Fasting blood glucose (FBG) (by self monitoring)
End point description:	
LS means were calculated using MMRM adjusting for stratification factors (country, baseline HbA1c [$\leq 8.0\%$ and $> 8.0\%$], baseline LDL-C [< 100 mg/dL and ≥ 100 mg/dL], and SU or meglitinide use), visit, treatment, visit-by-treatment interaction, and baseline FBG.	

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

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	303 ^[15]	158 ^[16]		
Units: milligrams per deciliter (mg/dL)				
least squares mean (standard error)				
26 weeks	106.32 (± 1.08)	104.50 (± 1.51)		
52 weeks	110.61 (± 1.19)	107.46 (± 1.68)		

Notes:

[15] - Randomized participant who received at least 1 dose of study drug and had evaluable FBG data.

[16] - Randomized participant who received at least 1 dose of study drug and had evaluable FBG data.

Statistical analyses

No statistical analyses for this end point

Secondary: Intra-participant variability in fasting blood glucose (FBG)

End point title	Intra-participant variability in fasting blood glucose (FBG)
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 the stratification factors (country, baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], baseline LDL-C [< 100 mg/dL and ≥ 100 mg/dL], and SU or meglitinide use), treatment, visit, treatment-by-visit interaction, and baseline FBG intra-participant variability.	
End point type	Secondary
End point timeframe:	
26 and 52 weeks	

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302 ^[17]	158 ^[18]		
Units: mg/dL				
least squares mean (standard error)				
26 weeks	13.70 (± 0.57)	17.90 (± 0.80)		
52 weeks	14.18 (± 0.65)	17.38 (± 0.91)		

Notes:

[17] - Randomized participants who had at least 1 dose of study drug and evaluable FBG data.

[18] - Randomized participants who had at least 1 dose of study drug and evaluable FBG data.

Statistical analyses

Secondary: 6-point self-monitored blood glucose (SMBG)

End point title	6-point self-monitored blood glucose (SMBG)
End point description:	
SMBG measurements were taken at 6 time points (pre-morning meal [fasting], pre-midday meal, pre-evening meal, bedtime, approximately 0300 hours, and pre-morning meal [fasting] on the next day) and were performed on 2 non-consecutive days in the week prior to next office visit. 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 ≥ 100 mg/dL], and SU or meglitinide use), visit, treatment, visit-by-treatment interaction, and baseline BG values.	
End point type	Secondary
End point timeframe:	
26 and 52 weeks	

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	288 ^[19]	148 ^[20]		
Units: mg/dL				
least squares mean (standard error)				
Pre-morning meal, 26 weeks (n=288, 148)	107.93 (\pm 1.30)	104.11 (\pm 1.83)		
Pre-midday meal, 26 weeks (n=287, 145)	120.87 (\pm 2.20)	132.56 (\pm 3.11)		
Pre-evening meal, 26 weeks (n=287, 146)	125.87 (\pm 2.18)	141.45 (\pm 3.08)		
Bedtime, 26 weeks (n=285, 143)	146.54 (\pm 2.61)	161.48 (\pm 3.69)		
0300 hours, 26 weeks (n=281, 142)	118.43 (\pm 2.04)	120.42 (\pm 2.87)		
Pre-morning meal next day, 26 weeks (n=288, 148)	106.28 (\pm 1.36)	102.79 (\pm 1.90)		
Pre-morning meal, 52 weeks (n=288, 148)	110.84 (\pm 1.39)	108.22 (\pm 1.94)		
Pre-midday meal, 52 weeks (n=287, 145)	121.34 (\pm 2.17)	130.55 (\pm 3.06)		
Pre-evening meal, 52 weeks (n=287, 146)	128.53 (\pm 2.00)	141.31 (\pm 2.82)		
Bedtime, 52 weeks (n=285, 143)	146.92 (\pm 2.37)	161.83 (\pm 3.34)		
0300 hours, 52 weeks (n=281, 142)	122.23 (\pm 1.96)	121.07 (\pm 2.76)		
Pre-morning meal next day, 52 weeks (n=288, 148)	110.38 (\pm 1.41)	106.68 (\pm 1.97)		

Notes:

[19] - Randomized participant who received at least 1 dose of study drug and had evaluable SMBG data.

[20] - Randomized participant who received at least 1 dose of study drug and had evaluable SMBG data.

Statistical analyses

No statistical analyses for this end point

Secondary: HbA1c

End point title	HbA1c
End point description: LS means were calculated using MMRM adjusting for stratification factors (country, baseline LDL-C [<100 mg/dL and ≥ 100 mg/dL], and SU or meglitinide use), visit, treatment, visit-by-treatment interaction, and baseline HbA1c.	
End point type	Secondary
End point timeframe: 26 and 52 weeks	

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302 ^[21]	157 ^[22]		
Units: percentage of HbA1c				
least squares mean (standard error)				
26 weeks	6.60 (± 0.04)	7.13 (± 0.06)		
52 weeks	6.75 (± 0.05)	7.20 (± 0.06)		

Notes:

[21] - Randomized participants who received at least 1 dose of study drug and had evaluable HbA1c data.

[22] - Randomized participants who received at least 1 dose of study drug and had evaluable HbA1c data.

Statistical analyses

No statistical analyses for this end point

Secondary: Insulin dose per kilogram of body weight

End point title	Insulin dose per kilogram of body weight
End point description: Daily basal insulin dose is presented. LS means were calculated using MMRM adjusting for the stratification factors (country, baseline HbA1c [$\leq 8.5\%$ and $>8.5\%$], baseline LDL-C [<100 mg/dL and ≥ 100 mg/dL], and SU or meglitinide use), treatment, visit, treatment-by-visit interaction, and baseline insulin dose.	
End point type	Secondary
End point timeframe: 26 and 52 weeks	

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304 ^[23]	159 ^[24]		
Units: units per kilogram per day (U/kg/day)				
least squares mean (standard error)				
26 weeks	0.57 (± 0.01)	0.49 (± 0.01)		
52 weeks	0.57 (± 0.01)	0.49 (± 0.02)		

Notes:

[23] - Randomized participants who received at least 1 dose of study drug and had evaluable data.

[24] - Randomized participants who received at least 1 dose of study drug and had evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of insulin dose adjustments to steady-state

End point title	Number of insulin dose adjustments to steady-state
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End point description:

The number of dose adjustments required to reach a steady dose is presented. LS means were calculated from negative binomial regression models, where the number of dose adjustments = treatment + stratification factors (country, baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], baseline LDL-C [< 100 mg/dL and ≥ 100 mg/dL], and SU or meglitinide use).

End point type	Secondary
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End point timeframe:

Baseline through 26 weeks

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304 ^[25]	159 ^[26]		
Units: number of dose adjustments				
least squares mean (standard error)	4.06 (\pm 0.16)	2.75 (\pm 0.20)		

Notes:

[25] - Randomized participants who received at least 1 dose of study drug and had evaluable data.

[26] - Randomized participants who received at least 1 dose of study drug and had evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: European Quality of Life - 5 Dimension (EuroQol-5D) score

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

The EuroQol-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 an analysis of covariance (ANCOVA) model adjusting for treatment, stratification factors (country, baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], and SU or meglitinide use), and baseline EuroQol-5D score.

End point type	Secondary
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End point timeframe:

26 weeks

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290 ^[27]	146 ^[28]		
Units: units on a scale				
least squares mean (standard error)	0.87 (± 0.01)	0.88 (± 0.01)		

Notes:

[27] - Randomized participants who received at least 1 dose of study drug and had evaluable data.

[28] - Randomized participants who received at least 1 dose of study drug and had evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Insulin Treatment Satisfaction Questionnaire (ITSQ) score

End point title	Insulin Treatment Satisfaction Questionnaire (ITSQ) score
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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, Insulin Delivery Device. Data presented are the transformed overall score on a scale of 0-100, where a higher score indicate better treatment satisfaction. LS means were calculated using ANCOVA with treatment and stratification factors (country, baseline HbA1c [$\leq 8.5\%$ and $>8.5\%$], and SU or meglitinide use) as fixed effects and baseline value of the ITSQ score as a covariate.

End point type	Secondary
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End point timeframe:

26 weeks

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	291 ^[29]	148 ^[30]		
Units: units on a scale				
least squares mean (standard error)	85.69 (± 0.63)	84.43 (± 0.89)		

Notes:

[29] - Randomized participants who received at least 1 dose of study drug and had evaluable data.

[30] - Randomized participants who received at least 1 dose of study drug and had evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Adult Low Blood Sugar Survey (LBSS) score

End point title	Adult Low Blood Sugar Survey (LBSS) score
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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 ANCOVA with treatment and stratification factors (country, baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], and SU or meglitinide use) as fixed effects and baseline value of the LBSS score as a covariate.

End point type	Secondary
End point timeframe:	
26 weeks	

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	292 ^[31]	148 ^[32]		
Units: units on a scale				
least squares mean (standard error)	16.57 (\pm 0.77)	15.63 (\pm 1.08)		

Notes:

[31] - Randomized participants who received at least 1 dose of study drug and had evaluable data.

[32] - Randomized participants who received at least 1 dose of study drug and had evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in body weight

End point title	Change from baseline in body weight
End point description:	
LS means were calculated using MMRM adjusting for stratification factors (country, baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], LDL-C [< 100 mg/dL and ≥ 100 mg/dL, except for the LDL-C outcome variable], and SU or meglitinide use), visit, treatment, visit-by-treatment interaction, and baseline body weight.	
End point type	Secondary
End point timeframe:	
Baseline, 26 weeks, 52 weeks	

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	303 ^[33]	157 ^[34]		
Units: kilograms (kg)				
least squares mean (standard error)				
26 weeks	0.50 (\pm 0.17)	0.94 (\pm 0.24)		
52 weeks	0.69 (\pm 0.23)	1.32 (\pm 0.32)		

Notes:

[33] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

[34] - Randomized participants who received at least 1 dose of study drug and had post baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in lipid profile

End point title	Change from baseline in lipid profile
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 (country, baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], LDL-C [< 100 mg/dL and ≥ 100 mg/dL, except for the LDL-C outcome variable], and SU or meglitinide use), visit, treatment, visit-by-treatment interaction, and baseline value of corresponding lipid outcome variable.	
End point type	Secondary
End point timeframe: Baseline, 26 weeks, 52 weeks	

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302 ^[35]	157 ^[36]		
Units: mg/dL				
least squares mean (standard error)				
Cholesterol, 26 weeks	2.24 (± 1.60)	3.70 (± 2.25)		
Cholesterol, 52 weeks	-1.35 (± 1.63)	2.78 (± 2.29)		
HDL-C, 26 weeks	-1.74 (± 0.37)	-0.06 (± 0.52)		
HDL-C, 52 weeks	-3.52 (± 0.37)	-2.01 (± 0.51)		
LDL-C, 26 weeks	-0.05 (± 1.43)	4.54 (± 2.00)		
LDL-C, 52 weeks	-3.38 (± 1.45)	3.41 (± 2.03)		
Triglycerides, 26 weeks	22.53 (± 3.73)	-2.90 (± 5.23)		
Triglycerides, 52 week	27.39 (± 4.00)	12.02 (± 5.59)		

Notes:

[35] - Randomized participant who received at least 1 dose of study drug and had evaluable data.

[36] - Randomized participant who received at least 1 dose of study drug and had evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Change in anti-LY2605541 antibodies

End point title	Number of Participants With Change in anti-LY2605541 antibodies
End point description: The number 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.	
End point type	Secondary
End point timeframe: Baseline through 52 weeks	

End point values	Insulin Peglispro (LY2605541)	Insulin glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301 ^[37]	157 ^[38]		
Units: participants				
number (not applicable)	70	30		

Notes:

[37] - All randomized participants who received at least 1 dose of study drug and had evaluable data.

[38] - All randomized participants who received at least 1 dose of study drug and had evaluable data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to 52 weeks

Adverse event reporting additional description:

I2R-MC-BIDJ

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	Insulin Glargine
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Reporting group description:

Insulin glargine was administered by SQ injection once daily at bedtime for up to 52 weeks. Initial dose was based on dose of prestudy basal insulin and adjusted based on FBG.

Reporting group title	Insulin Peglispro (LY2605541)
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Reporting group description:

Insulin peglispro (LY2605541) was administered by SQ injection once daily at bedtime for up to 52 weeks. Initial dose based on prestudy basal insulin and adjusted based on FBG.

Serious adverse events	Insulin Glargine	Insulin Peglispro (LY2605541)	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 159 (13.84%)	35 / 305 (11.48%)	
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)			
endometrial adenocarcinoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pituitary tumour benign			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
prostate cancer			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
rectosigmoid cancer			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal cancer			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal cell carcinoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
transitional cell carcinoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
cardiac death			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
chest pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
multi-organ failure			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
non-cardiac chest pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
benign prostatic hyperplasia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ovarian cyst			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
prostatitis			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
uterine prolapse			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
asthma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
pulmonary hypertension			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
sleep apnoea syndrome			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
mental status changes			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hepatic enzyme increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
cardiac vein perforation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
fall			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
foot fracture			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
laceration			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lower limb fracture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
postoperative respiratory failure			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
acute myocardial infarction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	2 / 305 (0.66%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
angina pectoris			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
arrhythmia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
atrial fibrillation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrial thrombosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac arrest			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
cardiac failure			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
cardiac failure congestive			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

cardiac tamponade alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 159 (0.63%) 0 / 1 0 / 0	 0 / 305 (0.00%) 0 / 0 0 / 0		
cardio-respiratory arrest alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 159 (0.63%) 0 / 1 0 / 1	 0 / 305 (0.00%) 0 / 0 0 / 0		
coronary artery disease alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 2 / 159 (1.26%) 0 / 2 0 / 0	 1 / 305 (0.33%) 0 / 1 0 / 0		
coronary artery occlusion alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 159 (0.63%) 0 / 1 0 / 0	 0 / 305 (0.00%) 0 / 0 0 / 0		
myocardial infarction alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 2 / 159 (1.26%) 0 / 2 0 / 1	 0 / 305 (0.00%) 0 / 0 0 / 0		
sick sinus syndrome alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 159 (0.00%) 0 / 0 0 / 0	 1 / 305 (0.33%) 0 / 1 0 / 0		
ventricular fibrillation alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
cerebral artery stenosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoaesthesia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lacunar infarction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
subarachnoid haemorrhage			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
syncope			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
angle closure glaucoma			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
colitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
inguinal hernia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
urethral obstruction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
intervertebral disc disorder			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
tendon disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
arthritis bacterial			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cellulitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
erysipelas			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
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	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia staphylococcal alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory tract infection alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract infection alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
viral infection alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
hypoglycaemia alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypovolaemia alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Insulin Glargine	Insulin Peglispro (LY2605541)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	103 / 159 (64.78%)	223 / 305 (73.11%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenoma benign			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
basal cell carcinoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)	
occurrences (all)	0	2	
benign neoplasm of adrenal gland			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
colon adenoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
lipoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
melanocytic naevus			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	

monoclonal gammopathy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
seborrhoeic keratosis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
squamous cell carcinoma of skin alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	0 / 305 (0.00%) 0	
Vascular disorders			
aortic stenosis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
haematoma alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	2 / 305 (0.66%) 2	
hypertension alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	5 / 159 (3.14%) 5	8 / 305 (2.62%) 8	
hypertensive crisis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
intra-abdominal haematoma alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
peripheral coldness alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
varicose vein			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
Surgical and medical procedures			
angioplasty			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
atrial septal defect repair			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
cardiac ablation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
cardiac pacemaker insertion			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
cataract operation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	4 / 305 (1.31%)	
occurrences (all)	0	8	
colon polypectomy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	4 / 305 (1.31%)	
occurrences (all)	0	4	
coronary angioplasty			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
coronary arterial stent insertion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
coronary artery bypass		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
debridement		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
endodontic procedure		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
gastric bypass		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
gastrostomy tube insertion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
hysterectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
inguinal hernia repair		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1

intervertebral disc operation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
intraocular lens implant alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	0 / 305 (0.00%) 0	
leg amputation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	0 / 305 (0.00%) 0	
limb operation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
medical device removal alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	0 / 305 (0.00%) 0	
mitral valve repair alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	0 / 305 (0.00%) 0	
oral surgery alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
osteosynthesis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
osteotomy alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	2
percutaneous coronary intervention		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
peripheral nerve operation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
polypectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
salpingo-oophorectomy bilateral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
sigmoidectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
spinal fusion surgery		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
strabismus correction		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
tendon sheath incision		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1

tendon transfer		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
tenotomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
thoracotomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
thyroidectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
toe amputation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
tooth extraction		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	3 / 305 (0.98%)
occurrences (all)	0	3
tracheostomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
transurethral prostatectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
uterine dilation and curettage		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
vitrectomy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
chest pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)	
occurrences (all)	1	2	
early satiety			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
face oedema			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
fatigue			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	4 / 159 (2.52%)	3 / 305 (0.98%)	
occurrences (all)	4	3	
inflammation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
influenza like illness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)	
occurrences (all)	1	2	
injection site hypertrophy			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
injection site injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
injection site nodule		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
injection site oedema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
injection site reaction		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
injury associated with device		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
malaise		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
non-cardiac chest pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
oedema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1

<p>oedema peripheral</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 159 (1.26%)</p> <p>2</p>	<p>5 / 305 (1.64%)</p> <p>5</p>	
<p>pain</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 159 (1.26%)</p> <p>2</p>	<p>0 / 305 (0.00%)</p> <p>0</p>	
<p>polyp</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>pyrexia</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>Immune system disorders</p> <p>allergy to arthropod sting</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>drug hypersensitivity</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>food allergy</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>0 / 159 (0.00%)</p> <p>0</p> <p>1 / 159 (0.63%)</p> <p>1</p> <p>0 / 159 (0.00%)</p> <p>0</p> <p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p> <p>1 / 305 (0.33%)</p> <p>1</p> <p>1 / 305 (0.33%)</p> <p>1</p>	

subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	3 / 305 (0.98%) 3	
Reproductive system and breast disorders			
balanoposthitis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
benign prostatic hyperplasia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	1 / 305 (0.33%) 1	
cystocele alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
dysmenorrhoea alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 3	0 / 305 (0.00%) 0	
erectile dysfunction alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	1 / 305 (0.33%) 1	
genital discomfort alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
metrorrhagia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 2	
ovarian cyst alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)	
occurrences (all)	0	3	
postmenopausal haemorrhage			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)	
occurrences (all)	0	2	
prostatitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
sexual dysfunction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
asthma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	1 / 305 (0.33%)	
occurrences (all)	2	1	
cough			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	9 / 159 (5.66%)	16 / 305 (5.25%)	
occurrences (all)	9	17	
dysphonia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)	
occurrences (all)	1	2	
dyspnoea			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	2 / 159 (1.26%)	2 / 305 (0.66%)
occurrences (all)	2	2
dyspnoea exertional		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
epistaxis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	3 / 305 (0.98%)
occurrences (all)	2	3
haemoptysis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
nasal congestion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
oropharyngeal pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	7 / 159 (4.40%)	6 / 305 (1.97%)
occurrences (all)	8	6
paranasal sinus hypersecretion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
productive cough		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)
occurrences (all)	1	2
pulmonary congestion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1

respiratory tract congestion alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	2 / 305 (0.66%) 2	
rhinitis allergic alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	2 / 305 (0.66%) 2	
rhinorrhoea alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	1 / 305 (0.33%) 1	
sinus congestion alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	5 / 305 (1.64%) 5	
sleep apnoea syndrome alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	1 / 305 (0.33%) 1	
throat irritation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	2 / 305 (0.66%) 2	
Psychiatric disorders anxiety alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	5 / 159 (3.14%) 5	2 / 305 (0.66%) 2	
depression alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 159 (1.26%) 2	4 / 305 (1.31%) 4	
insomnia alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	4 / 305 (1.31%)	
occurrences (all)	0	4	
mood altered			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
mood swings			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
neurosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
panic attack			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
sleep disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
stress			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)	
occurrences (all)	1	2	
arteriogram coronary			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
arthroscopy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
aspartate aminotransferase increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
biopsy skin		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
blood cholesterol increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
blood creatine phosphokinase increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
blood creatinine increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
blood iron decreased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
blood lactate dehydrogenase increased		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
blood potassium abnormal alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
blood potassium increased alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
blood pressure increased alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
blood uric acid increased alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	3 / 305 (0.98%)
occurrences (all)	0	3
carotid bruit alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
catheterisation cardiac alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	0 / 305 (0.00%)
occurrences (all)	2	0
colonoscopy alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
electrocardiogram st segment depression alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0

electrocardiogram t wave abnormal			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
endoscopy upper gastrointestinal tract			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
heart rate irregular			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
hepatic enzyme increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)	
occurrences (all)	0	2	
international normalised ratio increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
intraocular pressure increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
liver function test abnormal			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
low density lipoprotein increased			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
prostatic specific antigen increased			
alternative dictionary used: MedDRA 16.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>serum ferritin increased</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>weight decreased</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 159 (0.63%)</p> <p>1</p>	<p>0 / 305 (0.00%)</p> <p>0</p>	
<p>Injury, poisoning and procedural complications</p> <p>acetabulum fracture</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>arthropod bite</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>arthropod sting</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 159 (0.63%)</p> <p>1</p>	<p>0 / 305 (0.00%)</p> <p>0</p>	
<p>bite</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>bone contusion</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>contusion</p> <p>alternative dictionary used: MedDRA 16.0</p>			

subjects affected / exposed	3 / 159 (1.89%)	4 / 305 (1.31%)
occurrences (all)	3	4
epicondylitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)
occurrences (all)	1	2
excoriation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 159 (1.89%)	0 / 305 (0.00%)
occurrences (all)	4	0
eye injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
fall		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
foot fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
fractured coccyx		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
heat exhaustion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	2	0
joint injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1

ligament sprain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
limb injury			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	0 / 305 (0.00%)	
occurrences (all)	2	0	
limb traumatic amputation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
meniscus injury			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
muscle rupture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
muscle strain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	2 / 305 (0.66%)	
occurrences (all)	2	2	
nail avulsion			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
post-traumatic neck syndrome			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
procedural pain			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
rib fracture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
road traffic accident			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
scratch			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	2	0	
tendon rupture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
thermal burn			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
upper limb fracture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
wound			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
Congenital, familial and genetic disorders			
atrial septal defect			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	0 / 305 (0.00%) 0	
Cardiac disorders			
atrial fibrillation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	2 / 305 (0.66%)	
occurrences (all)	2	2	
bradycardia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
bundle branch block right			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
cardiac failure congestive			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 159 (1.89%)	0 / 305 (0.00%)	
occurrences (all)	3	0	
cardiomegaly			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
left ventricular dysfunction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
left ventricular hypertrophy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
mitral valve incompetence			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)	
occurrences (all)	1	1	
supraventricular extrasystoles			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
systolic dysfunction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
tachycardia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
ventricular extrasystoles			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)	
occurrences (all)	0	2	
Nervous system disorders			
carpal tunnel syndrome			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	4 / 305 (1.31%)	
occurrences (all)	0	4	
cerebral atrophy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
cervical myelopathy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
cervicobrachial syndrome			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
cubital tunnel syndrome		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
dementia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
diabetic neuropathy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
dizziness		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 159 (3.14%)	7 / 305 (2.30%)
occurrences (all)	6	8
headache		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	12 / 159 (7.55%)	17 / 305 (5.57%)
occurrences (all)	27	26
hypoesthesia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)
occurrences (all)	1	3
leukoencephalopathy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
memory impairment		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0

migraine		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	0 / 305 (0.00%)
occurrences (all)	5	0
neuropathy peripheral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
paraesthesia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 159 (1.89%)	4 / 305 (1.31%)
occurrences (all)	3	4
radiculitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
sciatica		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	3 / 305 (0.98%)
occurrences (all)	0	3
sinus headache		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	4	1
syncope		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
tremor		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
viith nerve paralysis		
alternative dictionary used: MedDRA 16.0		

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>with nerve paralysis</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p> <p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p> <p>1 / 305 (0.33%)</p> <p>1</p>	
<p>Blood and lymphatic system disorders</p> <p>anaemia</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>leukopenia</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>macrocytosis</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>splenomegaly</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>thrombocytopenia</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>5 / 159 (3.14%)</p> <p>5</p> <p>0 / 159 (0.00%)</p> <p>0</p> <p>1 / 159 (0.63%)</p> <p>1</p> <p>0 / 159 (0.00%)</p> <p>0</p> <p>0 / 159 (0.00%)</p> <p>0</p>	<p>3 / 305 (0.98%)</p> <p>3</p> <p>1 / 305 (0.33%)</p> <p>1</p> <p>0 / 305 (0.00%)</p> <p>0</p> <p>1 / 305 (0.33%)</p> <p>1</p> <p>1 / 305 (0.33%)</p> <p>1</p>	
<p>Ear and labyrinth disorders</p> <p>deafness unilateral</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>ear pain</p> <p>alternative dictionary used: MedDRA 16.0</p>	<p>1 / 159 (0.63%)</p> <p>1</p>	<p>0 / 305 (0.00%)</p> <p>0</p>	

subjects affected / exposed	3 / 159 (1.89%)	2 / 305 (0.66%)	
occurrences (all)	3	2	
hypoacusis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
presbycusis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
tinnitus			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	4 / 305 (1.31%)	
occurrences (all)	0	4	
tympanic membrane perforation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
vertigo			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)	
occurrences (all)	1	2	
vertigo positional			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
Eye disorders			
age-related macular degeneration			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	3 / 305 (0.98%)	
occurrences (all)	0	3	
cataract			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	5 / 305 (1.64%)
occurrences (all)	0	6
conjunctivitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
dacryostenosis acquired		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
diabetic retinal oedema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
dry eye		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
eye pruritus		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
eye swelling		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
lacrimation increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
ocular discomfort		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1

refraction disorder alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
retinal haemorrhage alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	0 / 305 (0.00%) 0	
retinopathy hypertensive alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
vision blurred alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
vitreous floaters alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	0 / 305 (0.00%) 0	
Gastrointestinal disorders abdominal discomfort alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	4 / 305 (1.31%) 6	
abdominal distension alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	2 / 305 (0.66%) 2	
abdominal pain alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	3 / 159 (1.89%) 3	7 / 305 (2.30%) 9	
abdominal pain lower alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
abdominal pain upper		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 159 (2.52%)	4 / 305 (1.31%)
occurrences (all)	4	6
colitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
colitis microscopic		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
constipation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 159 (2.52%)	8 / 305 (2.62%)
occurrences (all)	4	8
defaecation urgency		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
dental caries		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
diarrhoea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 159 (3.14%)	19 / 305 (6.23%)
occurrences (all)	5	21
dry mouth		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1

duodenal ulcer			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
dyspepsia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	6 / 305 (1.97%)	
occurrences (all)	2	6	
enterocolitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
epigastric discomfort			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
faecal incontinence			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
flatulence			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
food poisoning			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)	
occurrences (all)	1	1	
gastric cyst			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
gastric polyps			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
gastritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	3 / 305 (0.98%)
occurrences (all)	0	3
gastrointestinal angiodysplasia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
gastrointestinal disorder		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
gastrooesophageal reflux disease		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
haematochezia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
haemorrhoids		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	3 / 305 (0.98%)
occurrences (all)	0	3
hypoaesthesia oral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
impaired gastric emptying		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1

irritable bowel syndrome		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
large intestine polyp		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
lip swelling		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
loose tooth		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
nausea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 159 (2.52%)	12 / 305 (3.93%)
occurrences (all)	7	13
oesophagitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
pancreatic cyst		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
pancreatic insufficiency		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
periodontal inflammation		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
rectal haemorrhage			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
rectal polyp			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
tooth disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
tooth impacted			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
toothache			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 159 (1.89%)	5 / 305 (1.64%)	
occurrences (all)	3	5	
umbilical hernia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
vomiting			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	9 / 305 (2.95%)	
occurrences (all)	3	10	
Hepatobiliary disorders			
biliary dyskinesia			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
cholelithiasis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	3 / 305 (0.98%)	
occurrences (all)	1	3	
hepatic cyst			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
hepatic steatosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	4 / 305 (1.31%)	
occurrences (all)	0	4	
hepatocellular injury			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
hepatosplenomegaly			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
hypertransaminasaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
portal vein dilatation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
actinic keratosis			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	2 / 159 (1.26%)	3 / 305 (0.98%)
occurrences (all)	2	3
alopecia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
dermal cyst		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)
occurrences (all)	1	2
dermatitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	3 / 305 (0.98%)
occurrences (all)	0	3
dermatitis contact		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	1 / 305 (0.33%)
occurrences (all)	2	1
diabetic foot		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
dry skin		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
ecchymosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
eczema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	3 / 305 (0.98%)
occurrences (all)	1	3

erythema			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
hyperkeratosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
ingrowing nail			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	3 / 305 (0.98%)	
occurrences (all)	1	3	
lentigo			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
lipodystrophy acquired			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
lipohypertrophy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)	
occurrences (all)	0	2	
night sweats			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
onycholysis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
pruritus			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)
occurrences (all)	2	2
psoriasis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
rash		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	10 / 305 (3.28%)
occurrences (all)	1	11
rash erythematous		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
rash generalised		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
rash papular		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
rosacea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
skin discolouration		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
skin fissures		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2

<p>skin hyperpigmentation</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>swelling face</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>urticaria</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
Renal and urinary disorders			
<p>acute prerenal failure</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>calculus bladder</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>dysuria</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>haematuria</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 159 (1.89%)</p> <p>3</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>microalbuminuria</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 159 (0.63%)</p> <p>1</p>	<p>2 / 305 (0.66%)</p> <p>2</p>	
<p>nephrolithiasis</p> <p>alternative dictionary used: MedDRA 16.0</p>			

subjects affected / exposed	2 / 159 (1.26%)	4 / 305 (1.31%)	
occurrences (all)	2	4	
proteinuria			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
renal atrophy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	
renal cyst			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
renal failure			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)	
occurrences (all)	0	2	
renal failure chronic			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	1 / 305 (0.33%)	
occurrences (all)	2	1	
urethral haemorrhage			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
urinary retention			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
Endocrine disorders			
autoimmune thyroiditis			
alternative dictionary used: MedDRA 16.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>hyperprolactinaemia</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>hypogonadism</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 159 (0.00%)</p> <p>0</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>hypothyroidism</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 159 (0.63%)</p> <p>1</p>	<p>1 / 305 (0.33%)</p> <p>1</p>	
<p>thyroid cyst</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 159 (0.63%)</p> <p>1</p>	<p>0 / 305 (0.00%)</p> <p>0</p>	
<p>Musculoskeletal and connective tissue disorders</p> <p>arthralgia</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>7 / 159 (4.40%)</p> <p>7</p>	<p>16 / 305 (5.25%)</p> <p>19</p>	
<p>arthritis</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 159 (1.89%)</p> <p>3</p>	<p>6 / 305 (1.97%)</p> <p>6</p>	
<p>back pain</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>11 / 159 (6.92%)</p> <p>13</p>	<p>21 / 305 (6.89%)</p> <p>22</p>	
<p>bone pain</p> <p>alternative dictionary used: MedDRA 16.0</p>			

subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
bursitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
chondropathy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
dupuytren's contracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
flank pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
foot deformity		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	2	0
intervertebral disc disorder		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
intervertebral disc protrusion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
intervertebral disc space narrowing		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1

joint swelling		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)
occurrences (all)	1	3
medial tibial stress syndrome		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
muscle spasms		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	2 / 305 (0.66%)
occurrences (all)	2	2
muscular weakness		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)
occurrences (all)	1	2
musculoskeletal disorder		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
musculoskeletal pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 159 (1.89%)	6 / 305 (1.97%)
occurrences (all)	4	6
myalgia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 159 (1.89%)	2 / 305 (0.66%)
occurrences (all)	3	2
neck pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
osteitis		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
osteoarthritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 159 (1.89%)	5 / 305 (1.64%)
occurrences (all)	3	6
osteochondrosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
pain in extremity		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	9 / 159 (5.66%)	7 / 305 (2.30%)
occurrences (all)	9	7
periarthritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	1 / 305 (0.33%)
occurrences (all)	2	1
plantar fasciitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
rotator cuff syndrome		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)
occurrences (all)	1	2
spinal disorder		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
spinal osteoarthritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1

tendon disorder alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	0 / 305 (0.00%) 0	
tendonitis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 159 (1.26%) 3	0 / 305 (0.00%) 0	
trigger finger alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	0 / 305 (0.00%) 0	
Infections and infestations abscess limb alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all) acute sinusitis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all) acute tonsillitis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all) bacterial infection alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all) bronchitis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all) cellulitis alternative dictionary used: MedDRA 16.0	0 / 159 (0.00%) 0 0 / 159 (0.00%) 0 1 / 159 (0.63%) 1 1 / 159 (0.63%) 1 5 / 159 (3.14%) 5	1 / 305 (0.33%) 1 1 / 305 (0.33%) 1 0 / 305 (0.00%) 0 0 / 305 (0.00%) 0 14 / 305 (4.59%) 14	

subjects affected / exposed	1 / 159 (0.63%)	5 / 305 (1.64%)
occurrences (all)	2	7
cystitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	3
diverticulitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	0 / 305 (0.00%)
occurrences (all)	2	0
ear infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	1 / 305 (0.33%)
occurrences (all)	2	1
erysipelas		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
fungus infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
fungus skin infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	2
gastroenteritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	1 / 305 (0.33%)
occurrences (all)	2	1
gastroenteritis viral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 159 (1.89%)	2 / 305 (0.66%)
occurrences (all)	3	2

helicobacter infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
herpes zoster		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	2 / 305 (0.66%)
occurrences (all)	2	2
hordeolum		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	2	0
infected cyst		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
influenza		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	11 / 159 (6.92%)	13 / 305 (4.26%)
occurrences (all)	13	14
laryngitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
localised infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	2	1
lower respiratory tract infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	3 / 305 (0.98%)
occurrences (all)	0	4
nail infection		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
nasal abscess		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
nasopharyngitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	27 / 159 (16.98%)	53 / 305 (17.38%)
occurrences (all)	33	68
onychomycosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
oral candidiasis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
oral fungal infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
oral herpes		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
orchitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
otitis media		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1

paronychia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
periodontitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	2	0
pharyngitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	1 / 305 (0.33%)
occurrences (all)	3	2
pharyngitis streptococcal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
pneumonia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	3 / 305 (0.98%)
occurrences (all)	1	3
post procedural infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
respiratory tract infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
respiratory tract infection viral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	3
rhinitis		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	2 / 159 (1.26%)	3 / 305 (0.98%)
occurrences (all)	2	3
sialoadenitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
sinusitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	9 / 159 (5.66%)	18 / 305 (5.90%)
occurrences (all)	9	19
staphylococcal infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
tinea infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1
tinea pedis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
tooth abscess		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	3 / 305 (0.98%)
occurrences (all)	0	3
tooth infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	5 / 305 (1.64%)
occurrences (all)	1	5
tracheobronchitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)
occurrences (all)	1	1

upper respiratory tract infection alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	8 / 159 (5.03%) 11	16 / 305 (5.25%) 18	
urinary tract infection alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	4 / 159 (2.52%) 5	7 / 305 (2.30%) 8	
viral infection alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	4 / 305 (1.31%) 7	
viral upper respiratory tract infection alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 159 (1.26%) 4	4 / 305 (1.31%) 4	
vulvovaginal mycotic infection alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	1 / 305 (0.33%) 1	
wound infection alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
Metabolism and nutrition disorders abnormal loss of weight alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 159 (0.00%) 0	1 / 305 (0.33%) 1	
acidosis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 159 (0.63%) 1	0 / 305 (0.00%) 0	
decreased appetite alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)
occurrences (all)	0	1
dehydration		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
dyslipidaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	0 / 305 (0.00%)
occurrences (all)	2	0
gout		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	3 / 305 (0.98%)
occurrences (all)	2	3
hyperglycaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 159 (1.26%)	0 / 305 (0.00%)
occurrences (all)	3	0
hyperkalaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0
hyperlipidaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	2 / 305 (0.66%)
occurrences (all)	1	2
hyperuricaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 159 (0.00%)	2 / 305 (0.66%)
occurrences (all)	0	2
hypokalaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)
occurrences (all)	1	0

iron deficiency			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	1 / 305 (0.33%)	
occurrences (all)	1	1	
obesity			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 159 (0.00%)	1 / 305 (0.33%)	
occurrences (all)	0	1	
vitamin b12 deficiency			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 159 (1.26%)	0 / 305 (0.00%)	
occurrences (all)	2	0	
vitamin d deficiency			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 159 (0.63%)	0 / 305 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported