Clinical trial results:
A Comparison of Pharmacodynamics When Receiving a Double Dose of Insulin Peglispro or Insulin Glargine in Patients with Type 2 Diabetes Mellitus: A Double-Blind, Crossover Design Study: The IMAGINE 8 Study

Summary

EudraCT number	2012-005174-56
Trial protocol	DE
Global end of trial date	10 July 2015

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	12R-MC-BIDD

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02132637
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 14288

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Eli Lilly and Company, Available Mon - Fri 9 AM - 5 PM EST, 1 877-285-4559,
Scientific contact	Eli Lilly and Company, Available Mon - Fri 9 AM - 5 PM EST, 1 877-CTLilly,

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	10 July 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that clinically significant hypoglycemia (defined as blood glucose <54 mg/dL (3.0 mmol/L) or symptoms of severe hypoglycemia) is significantly less frequent following a double dose of insulin peglispro than following a double dose of insulin glargine within 84 hours of double dosing in patients with Type 2 Diabetes Mellitus (T2DM).

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	19 May 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 10
Country: Number of subjects enrolled	Germany: 58
Worldwide total number of subjects	68
EEA total number of subjects	58

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	56
From 65 to 84 years	12

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

No Text Entered

Pre-assignment

Screening details:

No Text Entered

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Insulin Peglispro/Insulin Glargine

Arm description:

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in the first study period. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in the second study period. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

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:

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in the first study period. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

Arm title	Insulin Glargine/Insulin Peglispro

Arm description:

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in the first study period. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in the second study period. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

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

Dosage and administration details:

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in the first study period. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

Number of subjects in period 1	Insulin Peglispro/Insulin Glargine	Insulin Glargine/Insulin Peglispro
Started	34	34
Completed	33	30
Not completed	1	4
Physician decision	1	-
Withdrawn by subject	-	4

Period 2

Period 2 title	Study Period 2 (Crossover)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Insulin Peglispro/Insulin Glargine

Arm description:

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in the first study period. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in the second study period. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

Arm type	Experimental
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:

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in the second study period. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

Arm title	Insulin Glargine/Insulin Peglispro

Arm description:

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in the first study period. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in the second study period. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

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:

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in the second study period. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

Number of subjects in period 2	Insulin Peglispro/Insulin Glargine	Insulin Glargine/Insulin Peglispro
Started	33	30
Completed	31	29
Not completed	2	1
Physician decision	2	-
Withdrawn by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Insulin Peglispro/Insulin Glargine

Reporting group description:

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in the first study period. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in the second study period. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

Reporting group title	Insulin Glargine/Insulin Peglispro

Reporting group description:

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in the first study period. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in the second study period. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

Reporting group values	Insulin Peglispro/Insulin Glargine	Insulin Glargine/Insulin Peglispro	Total
Number of subjects	34	34	68
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	57.82	57.74	
standard deviation	± 8.06	± 5.86	-
Gender categorical Units: Subjects			
Female	10	10	20
Male	24	24	48
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	5	9
Not Hispanic or Latino	30	29	59
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	1
Native Hawaiian or Other	1	0	1
Black or African American	0	0	0
White	32	34	66
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Insulin Peglispro/Insulin Glargine

Reporting group description:

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in the first study period. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in the second study period. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

Reporting group title	Insulin Glargine/Insulin Peglispro

Reporting group description:

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in the first study period. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in the second study period. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

Reporting group title	Insulin Peglispro/Insulin Glargine

Reporting group description:

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in the first study period. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in the second study period. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

Reporting group title	Insulin Glargine/Insulin Peglispro

Reporting group description:

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in the first study period. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in the second study period. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

Subject analysis set title	Insulin Peglispro
Subject analysis set type	Full analysis

Subject analysis set description:

Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in one of two study periods. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.

Subject analysis set title	Insulin Glargine
Subject analysis set type	Full analysis

Subject analysis set description:

Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in one of two study periods. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.

Primary: Percentage of Participants With Clinically Significant Hypoglycemia

End point title	Percentage of Participants With Clinically Significant Hypoglycemia[1]

End point description:

The percentage was calculated by dividing the number of participants with clinically significant hypoglycemia events defined as blood glucose <54 milligrams per deciliter (mg/dL) (3.0 millimole per liter [mmol/L]) or symptoms of severe hypoglycemia by the total number of participants analyzed, multiplied by 100.

Analysis Population Description: All randomized participants who received the double dose of study drug and had evaluable hypoglycemia data were included in the analysis.

End point type	Primary

End point timeframe:

Predose to 84 Hours Post Double Dose

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: System limitation- cannot accurately enter the number of participants enrolled in each treatment arm of this cross-over design. The statistical analysis included a total 62 participants. The method was a generalized linear model with fixed effect of treatment, period, sequence and baseline basal insulin dose strata, and random effect of participant. The P-value was <.001. The odds ratio was 0.13 at 95% confidence interval (0.04, 0.39).

End point values	Insulin Peglispro	Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	61	62		
Units: percentage of participants				
number (not applicable)	6.6	35.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Clinically Significant Hypoglycemia 12 Hours Post Double Dose

End point title	Percentage of Participants With Clinically Significant Hypoglycemia 12 Hours Post Double Dose

End point description:

The percentage was calculated by dividing the number of participants with clinically significant hypoglycemia events defined as blood glucose <54 mg/dL (3.0 mmol/L) or symptoms of severe hypoglycemia by the total number of participants analyzed, multiplied by 100.

Analysis Population Description: All randomized participants who received the double dose of study drug and had evaluable hypoglycemia data were included in the analysis.

End point type	Secondary

End point timeframe:

Predose to 12 Hours Post Double Dose

End point values	Insulin Peglispro	Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	61	62		
Units: percentage of participants				
number (not applicable)	1.6	22.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Hypoglycemia

End point title	Percentage of Participants With Hypoglycemia

End point description:

The percentage was calculated by dividing the number of participants with hypoglycemia events defined as blood glucose ≤70 mg/dL (3.9 mmol/L) by the total number of participants analyzed, multiplied by 100.

Analysis Population Description: All randomized participants who received the double dose of study drug and had evaluable hypoglycemia data were included in the analysis.

End point type	Secondary

End point timeframe:

Predose to 12 Hours Post Double Dose and 84 Hours Post Double Dose

End point values	Insulin Peglispro	Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	61	62		
Units: percentage of participants				
number (not applicable)				
12 Hours Post Double Dose	19.7	64.5		
84 Hours Post Double Dose	42.6	82.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Nadir Glucose

End point title	Nadir Glucose

End point description:

Nadir glucose was defined as the lowest blood glucose for a participant with blood glucose ≤70 mg/dL (3.9 mmol/L). Least Squares (LS) means were calculated using a mixed model repeated measures (MMRM) analysis including the following fixed effects: treatment, period, sequence, and baseline basal insulin dose stratification factor.

Analysis Population Description: All randomized participants who received the double dose of study drug and had blood glucose ≤70 mg/dL (3.9 mmol/L) during the first 84 hours after the double dose were included in the analysis.

End point type	Secondary

End point timeframe:

Predose to 84 Hours Post Double Dose

End point values	Insulin Peglispro	Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	51		
Units: mg/dL				
least squares mean (standard error)	61.7 (± 1.36)	55.93 (± 0.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to the Nadir Glucose

End point title	Time to the Nadir Glucose

End point description:

Nadir glucose was defined as the lowest blood glucose for a participant with blood glucose ≤70 mg/dL (3.9 mmol/L). The average time was calculated by dividing the sum of time from double dose to the nadir glucose for participants with blood glucose ≤70 mg/dL (3.9 mmol/L) by the number of participants with blood glucose ≤70 mg/dL (3.9 mmol/L) during the first 84 hours after the double dose.

Analysis Population Description: All randomized participants who received the double dose of study drug and had blood glucose ≤70 mg/dL (3.9 mmol/L) during the first 84 hours after the double dose were included in the analysis.

End point type	Secondary

End point timeframe:

Predose to 84 Hours Post Double Dose

End point values	Insulin Peglispro	Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	51		
Units: hours				
median (full range (min-max))	27.93 (3.17 to 76.67)	27.33 (1.00 to 81.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Glucose ≤70 mg/dL

End point title	Duration of Glucose ≤70 mg/dL

End point description:

The duration in minutes of each hypoglycemia episode with glucose ≤70 mg/dL (3.9 mmol/L) was calculated from start time to end time. The duration for a participant was the sum of the durations over the multiple hypoglycemia episodes. LS means were calculated using an MMRM analysis including the following fixed effects: treatment, period, sequence, and baseline basal insulin dose stratification factor.

Analysis Population Description: All randomized participants who received the double dose of study drug and had evaluable hypoglycemia data were included in the analysis.

End point type	Secondary

End point timeframe:

Predose to 84 Hours Post Double Dose

End point values	Insulin Peglispro	Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	61	62		
Units: Minutes per participant				
least squares mean (standard error)	95.28 (± 37.57)	362.26 (± 37.26)		

Statistical analyses

No statistical analyses for this end point

Secondary: Fasting Blood Glucose

End point title	Fasting Blood Glucose

End point description:

Fasting blood glucose (FBG) was measured by self-monitored blood glucose. LS means were calculated by MMRM analysis with fixed effects of treatment, dosing day, sequence, period, interaction of treatment and dosing day, baseline basal insulin dose stratification factor, and baseline FBG.

Analysis Population Description: All randomized participants who received the double dose of study drug and had evaluable fasting blood glucose data were included in the analysis.

End point type	Secondary

End point timeframe:

Day 1, Day 2, and Day 3 Following Double Dose

End point values	Insulin Peglispro	Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	62	62		
Units: mg/dL				
least squares mean (standard error)				
Day 1 (n=61, 62)	102.03 (± 2.9)	85.61 (± 2.87)		
Day 2 (n=62, 61)	100.94 (± 2.92)	86.16 (± 2.91)		
Day 3 (n=62, 61)	102.18 (± 2.99)	86.27 (± 3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics: Three-Hour Postprandial Glucose Area Under the Concentration Time Curve (AUC)

End point title	Pharmacodynamics: Three-Hour Postprandial Glucose Area Under the Concentration Time Curve (AUC)

End point description:

Glucose AUC within 3 hours after each meal assessed by the AUC of glucose from preprandial to 3 hours postprandial. LS means were calculated using an MMRM analysis including the following fixed effects: treatment, period, sequence, and baseline basal insulin dose stratification factor.

Analysis Population Description: All randomized participants who received at least one dose of study drug and had evaluable glucose data were included in the analysis.

End point type	Secondary

End point timeframe:

Preprandial to 3 Hours Postprandial during the day following the standard dose

End point values	Insulin Peglispro	Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	62	63		
Units: mg/dL*h				
least squares mean (standard error)				
Breakfast (n=62, 63)	633.5 (± 15.59)	568.64 (± 15.51)		
Lunch (n=62, 63)	566 (± 19.92)	568.2 (± 19.84)		
Dinner (n=62, 62)	564.68 (± 15.95)	577.46 (± 15.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacodynamics: Three-Hour Postprandial Glucose Area Under the Concentration Time Curve (AUC) Excursion

End point title	Pharmacodynamics: Three-Hour Postprandial Glucose Area Under the Concentration Time Curve (AUC) Excursion

End point description:

Glucose AUC excursion within 3 hours after each meal assessed by the AUC of adjusted glucose (= observed glucose - preprandial glucose) from preprandial to 3 hours postprandial. LS means were calculated using an MMRM analysis including the following fixed effects: treatment, period, sequence, and baseline basal insulin dose stratification factor.

Analysis Population Description: All randomized participants who received at least one dose of study drug and had evaluable glucose data were included in the analysis.

End point type	Secondary

End point timeframe:

Preprandial to 3 Hours Postprandial during the day following the standard dose

End point values	Insulin Peglispro	Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	62	63		
Units: mg/dL*h				
least squares mean (standard error)				
Breakfast (n=62, 63)	266.33 (± 12.04)	270.32 (± 11.98)		
Lunch (n=62, 63)	-2.38 (± 11.42)	36.92 (± 11.34)		
Dinner (n=62, 62)	134.4 (± 10.2)	150.23 (± 10.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Beta Cell Function

End point title	Beta Cell Function

End point description:

Beta cell function assessed by the change between pre meal tolerance test and 30 minutes post meal tolerance test in C-peptide corrected insulin/Glucose (ΔC-peptide corrected insulin/ΔGlucose). LS means were calculated using an MMRM analysis including the following fixed effects: treatment, period, sequence, and baseline basal insulin dose stratification factor.

Analysis Population Description: All randomized participants who received at least one dose of study drug and had evaluable ΔC-peptide data were included in the analysis.

End point type	Secondary

End point timeframe:

0-30 minutes during the meal tolerance test on the day following the standard dose

End point values	Insulin Peglispro	Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	67		
Units: pmol/L/(mmol/L)				
least squares mean (standard error)	88.65 (± 8.43)	103.62 (± 8.32)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Analysis Period 2 (AP2)	
Adverse event reporting additional description:	
I2R-MC-BIDD	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	Insulin Glargine
Reporting group description:	
Standard dose of insulin glargine administered subcutaneously (SQ) once daily for 4 weeks in one of two study periods. Double dose of insulin glargine administered once, SQ on day 3 of the inpatient stay.	
Reporting group title	Insulin Peglispro
Reporting group description:	
Standard dose of insulin peglispro administered subcutaneously (SQ) once daily for 4 weeks in one of two study periods. Double dose of insulin peglispro administered once, SQ on day 3 of the inpatient stay.	

Serious adverse events	Insulin Glargine	Insulin Peglispro	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 67 (1.49%)	2 / 64 (3.13%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
gastritis erosive			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 67 (0.00%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
otitis media			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Insulin Glargine	Insulin Peglispro	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 67 (38.81%)	31 / 64 (48.44%)	
Vascular disorders			
phlebitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
fatigue			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
infusion site extravasation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
peripheral swelling			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
rhinitis allergic			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
Psychiatric disorders			
irritability			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
ligament sprain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
Cardiac disorders			
tachycardia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	2	
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 67 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
headache			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	7 / 67 (10.45%)	11 / 64 (17.19%)	
occurrences (all)	7	16	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
deafness unilateral			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	

vertigo			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	2 / 64 (3.13%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	3 / 64 (4.69%)	
occurrences (all)	1	3	
constipation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 67 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
diarrhoea			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 67 (2.99%)	1 / 64 (1.56%)	
occurrences (all)	2	1	
nausea			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 67 (0.00%)	3 / 64 (4.69%)	
occurrences (all)	0	4	
vomiting			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 67 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
ecchymosis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	3 / 67 (4.48%)	2 / 64 (3.13%)	
occurrences (all)	5	3	
Renal and urinary disorders			
bladder pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 67 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
pollakiuria			

alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 67 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
arthritis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 67 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
back pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	4 / 67 (5.97%)	4 / 64 (6.25%)	
occurrences (all)	4	5	
joint swelling			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
myalgia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 67 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
pain in extremity			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	3 / 64 (4.69%)	
occurrences (all)	1	3	
Infections and infestations			
cellulitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
conjunctivitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 67 (2.99%)	0 / 64 (0.00%)	
occurrences (all)	2	0	
cystitis			
alternative dictionary used:			

MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
gastroenteritis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
nasopharyngitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	6 / 67 (8.96%)	5 / 64 (7.81%)	
occurrences (all)	6	5	
oral herpes			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
paronychia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
rhinitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
upper respiratory tract infection			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 67 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
hyperglycaemia			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	1 / 67 (1.49%)	1 / 64 (1.56%)	
occurrences (all)	1	1	
hypoglycaemia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 67 (1.49%)	0 / 64 (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