Clinical trial results:
A Randomized, Open-label Study on the Effects of Insulin Pen Devices on Glycemic Control in Children, Adolescents and Adults with Type 1 Diabetes: Novel Pen with Memory Function (HumaPen Memoir) vs. Conventional Pen without Memory Function (HumaPen Luxura)

Summary

EudraCT number	2008-007769-21
Trial protocol	DE
Global end of trial date	18 July 2011

Results information

Result version number	v1 (current)
This version publication date	03 April 2019
First version publication date	03 April 2019

Trial information

Trial identification

Sponsor protocol code	H9D-SB-ITAE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00985712
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 12704

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 July 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 July 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to test the hypothesis that the HumaPen Memoir with memory function, when used over 24 weeks for prandial insulin injections achieves superior glycemic control, when compared to the conventional HumaPen Luxura without memory function.

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	28 September 2009
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	Germany: 257
Worldwide total number of subjects	257
EEA total number of subjects	257

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)	4
Adolescents (12-17 years)	25
Adults (18-64 years)	208
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Not applicable

Period 1

Period 1 title	Overall Study
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	HumaPen Luxura

Arm description:

Participant’s insulin dose of Insulin Lispro or Huminsulin Normal is delivered subcutaneously via HumaPen Luxura daily for 24 weeks

Arm type	Experimental
Investigational medicinal product name	Huminsulin Regular
Investigational medicinal product code	
Other name	Huminsulin Normal, LY041001
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participant's received insulin dose of Huminsulin Normal subcutaneously.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	Humalog, LY275585
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participant's received insulin dose of Insulin Lispro through subcutaneous route.

Arm title	HumaPen Memoir

Arm description:

Participant’s insulin dose of Insulin Lispro or Huminsulin Normal is delivered subcutaneously via HumaPen Memoir daily for 24 weeks

Arm type	Experimental
Investigational medicinal product name	Huminsulin Regular
Investigational medicinal product code	
Other name	Huminsulin Normal, LY041001
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participant's received insulin dose of Huminsulin Normal subcutaneously.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	Humalog, LY275585
Pharmaceutical forms	Solution for injection

Routes of administration	Subcutaneous use

Dosage and administration details:

Participant's received insulin dose of Insulin Lispro through subcutaneous route.

Number of subjects in period 1	HumaPen Luxura	HumaPen Memoir
Started	133	130
Received at Least One Dose of Study Drug	131	130
Full Analysis Set (FAS)	128	129
Completed	127	123
Not completed	6	7
Consent withdrawn by subject	4	1
Adverse event, non-fatal	-	1
Lost to follow-up	2	2
Sponsor decision	-	2
Protocol deviation	-	1

Period 2

Period 2 title	Full Analysis Set (FAS)
Is this the baseline period?	Yes[1]
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	HumaPen Luxura

Arm description:

Participant’s insulin dose of Insulin Lispro or Huminsulin Normal is delivered subcutaneously via HumaPen Luxura daily for 24 weeks

Arm type	Experimental
Investigational medicinal product name	Huminsulin Regular
Investigational medicinal product code	
Other name	Huminsulin Normal, LY041001
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participant's received insulin dose of Huminsulin Normal subcutaneously.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	Humalog, LY275585
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participant's received insulin dose of Insulin Lispro through subcutaneous route.

Arm title	HumaPen Memoir

Arm description:

Participant’s insulin dose of Insulin Lispro or Huminsulin Normal is delivered subcutaneously via HumaPen Memoir daily for 24 weeks

Arm type	Experimental
Investigational medicinal product name	Huminsulin Regular
Investigational medicinal product code	
Other name	Huminsulin Normal, LY041001
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participant's received insulin dose of Huminsulin Normal subcutaneously.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	Humalog, LY275585
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participant's received insulin dose of Insulin Lispro through subcutaneous route.

Notes:

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

Justification: The baseline characteristics are calculated for Full Analysis Set (FAS) participants as per SAP.

Number of subjects in period 2	HumaPen Luxura	HumaPen Memoir
Started	128	129
Completed	127	123
Not completed	1	6
Consent withdrawn by subject	1	-
Adverse event, non-fatal	-	1
Lost to follow-up	-	2
Sponsor decision	-	2
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	HumaPen Luxura
Reporting group description:	
Participant's insulin dose of Insulin Lispro or Huminsulin Normal is delivered subcutaneously via HumaPen Luxura daily for 24 weeks	
Reporting group title	HumaPen Memoir
Reporting group description:	
Participant's insulin dose of Insulin Lispro or Huminsulin Normal is delivered subcutaneously via HumaPen Memoir daily for 24 weeks	

Reporting group values	HumaPen Luxura	HumaPen Memoir	Total
Number of subjects	128	129	257
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: years			
arithmetic mean	41.2	38.3	
standard deviation	± 15.52	± 17.37	-
Gender, Male/Female Units: Participants			
Female	52	56	108
Male	76	73	149
Race/Ethnicity, Customized Units: Subjects			
White	127	128	255
Black or African American	1	1	2
Region of Enrollment Units: Subjects			
Germany	128	129	257
Hemoglobin A1c (HbA1c)			
HbA1c is a form of hemoglobin which is measured primarily to identify the average plasma glucose concentration over prolonged periods of time.			
Units: percentage of glycosylated hemoglobin			
arithmetic mean	9.06	9.12	
standard deviation	± 0.93	± 1.04	-

End points

End points reporting groups

Reporting group title	HumaPen Luxura
Reporting group description:	
Participant’s insulin dose of Insulin Lispro or Huminsulin Normal is delivered subcutaneously via HumaPen Luxura daily for 24 weeks	
Reporting group title	HumaPen Memoir
Reporting group description:	
Participant’s insulin dose of Insulin Lispro or Huminsulin Normal is delivered subcutaneously via HumaPen Memoir daily for 24 weeks	
Reporting group title	HumaPen Luxura
Reporting group description:	
Participant’s insulin dose of Insulin Lispro or Huminsulin Normal is delivered subcutaneously via HumaPen Luxura daily for 24 weeks	
Reporting group title	HumaPen Memoir
Reporting group description:	
Participant’s insulin dose of Insulin Lispro or Huminsulin Normal is delivered subcutaneously via HumaPen Memoir daily for 24 weeks	

Primary: Change from baseline in hemoglobin A1c (HbA1c) at week 24 endpoint

End point title	Change from baseline in hemoglobin A1c (HbA1c) at week 24 endpoint
End point description:	
HbA1c is a form of hemoglobin which is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. Least Squares (LS) Mean values were controlled for treatment, visit, treatment*visit interaction, screening HbA1c (≤9% / >9%), change of prandial insulin at baseline, and baseline HbA1c. Analysis Population Description: Participants in full analysis population set with missing values accounted for using mixed model repeated measures (MMRM).	
End point type	Primary
End point timeframe:	
Baseline, Week 24	

End point values	HumaPen Luxura	HumaPen Memoir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	129		
Units: percentage of glycosylated hemoglobin				
least squares mean (confidence interval 95%)	-0.48 (-0.64 to -0.32)	-0.43 (-0.59 to -0.28)		

Statistical analyses

Statistical analysis title	Hemoglobin A1c (HbA1c)
Statistical analysis description:	
Superiority criterion is met if the upper limit of Confidence Interval (CI) is below zero.	
Comparison groups	HumaPen Luxura v HumaPen Memoir
Number of subjects included in analysis	257
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6692
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.26
Variability estimate	Standard error of the mean
Dispersion value	0.11

Secondary: Percentage of participants achieving Hemoglobin A1c (HbA1c) ≤7.5% and ≤7.0% at week 24 endpoint

End point title	Percentage of participants achieving Hemoglobin A1c (HbA1c) ≤7.5% and ≤7.0% at week 24 endpoint
End point description:	
Analysis Population Description: Participants in full analysis population set who had Week 24 measurements.	
End point type	Secondary
End point timeframe:	
Week 24	

End point values	HumaPen Luxura	HumaPen Memoir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	127	127		
Units: percentage of participants				
number (not applicable)				
HbA1c ≤7.0%	5.5	3.1		
HbA1c ≤7.5%	16.5	11.0		

Statistical analyses

Statistical analysis title	Percentage of Participants Achieving HbA1c
Comparison groups	HumaPen Luxura v HumaPen Memoir

Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3551 [1]
Method	Chi-squared
Confidence interval	
level	95 %

Notes:

[1] - P-value is for HbA1c ≤7.0%.

Statistical analysis title	Percentage of Participants Achieving HbA1c
Comparison groups	HumaPen Luxura v HumaPen Memoir
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2026 [2]
Method	Chi-squared
Confidence interval	
level	95 %

Notes:

[2] - P-value is for HbA1c ≤7.5%.

Secondary: Score in Insulin Delivery System Questionnaire (IDSQ) - Willingness to continue at week 24 endpoint

End point title	Score in Insulin Delivery System Questionnaire (IDSQ) - Willingness to continue at week 24 endpoint

End point description:

IDSQ is used to evaluate acceptance of study pen. Willingness to continue was assessed by a single question, rated from 1 to 5 (1=Definitely unwilling and 5=Definitely willing). Higher score indicates stronger desire to continue. Least Squares (LS) Mean values were controlled for treatment and baseline score.
Analysis Population Description: Participants in full analysis population set who had Week 24 measurements.

End point type	Secondary

End point timeframe:

Week 24

End point values	HumaPen Luxura	HumaPen Memoir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	126		
Units: units on a scale				
least squares mean (confidence interval 95%)	4.06 (3.88 to 4.25)	4.05 (3.86 to 4.23)		

Statistical analyses

Statistical analysis title	Insulin Delivery System Questionnaire (IDSQ)
Comparison groups	HumaPen Luxura v HumaPen Memoir
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.907
Method	ANCOVA
Confidence interval	
level	95 %

Secondary: 30-Day adjusted rates of self-Reported hypoglycemic episodes at any time from baseline through week 24

End point title	30-Day adjusted rates of self-Reported hypoglycemic episodes at any time from baseline through week 24

End point description:

Hypoglycemic episode is defined as blood glucose measurement ≤3.9 millimoles/Liter (mmol/L; 70 milligrams/deciliter [mg/dL]). Adjusted rate = number of events in study period, divided by number of days in study period, then multiplied by 30.
Analysis Population Description: Randomized participants who took at least one dose of study drug with post-baseline hypoglycemia follow-up.

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	HumaPen Luxura	HumaPen Memoir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	130		
Units: number of events per 30 days				
arithmetic mean (standard deviation)	2.68 (± 4.66)	2.46 (± 4.38)		

Statistical analyses

Statistical analysis title	Hypoglycemic Episodes
Comparison groups	HumaPen Luxura v HumaPen Memoir
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9817
Method	Wilcoxon (Mann-Whitney)
Confidence interval	
level	95 %

Secondary: 30-Day adjusted rates of self-Reported hyperglycemic episodes at any time from baseline through week 24

End point title	30-Day adjusted rates of self-Reported hyperglycemic episodes at any time from baseline through week 24

End point description:

Hyperglycemic episode is defined as blood glucose measurement >18 mmol/L (324 mg/dL). Adjusted rate = number of events in study period, divided by number of days in study period, then multiplied by 30.
Analysis Population Description: Randomized participants who took at least one dose of study drug with post-baseline hyperglycemia follow-up.

End point type	Secondary

End point timeframe:

Baseline through Week 24

End point values	HumaPen Luxura	HumaPen Memoir		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	130		
Units: number of events per 30 days				
arithmetic mean (standard deviation)	2.56 (± 5.50)	3.92 (± 9.82)		

Statistical analyses

Statistical analysis title	Hypoglycemic Episodes
Comparison groups	HumaPen Luxura v HumaPen Memoir
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1187
Method	Wilcoxon (Mann-Whitney)
Confidence interval	
level	95 %

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

H9D-SB-ITAE

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	HumaPen Luxura
Reporting group description: -	
Reporting group title	HumaPen Memoir
Reporting group description: -	

Serious adverse events	HumaPen Luxura	HumaPen Memoir	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 131 (5.34%)	8 / 130 (6.15%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
glycosylated haemoglobin increased			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
road traffic accident			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper limb fracture			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
cerebrovascular accident			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
gastritis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
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			
cervical spinal stenosis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
cystitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 131 (1.53%)	0 / 130 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
salpingo-oophoritis			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper respiratory tract infection			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
diabetic foot			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	2 / 130 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
diabetic ketoacidosis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyperglycaemia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	1 / 130 (0.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoglycaemia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 131 (1.53%)	0 / 130 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	HumaPen Luxura	HumaPen Memoir	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 131 (39.69%)	50 / 130 (38.46%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
benign ovarian tumour			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
Vascular disorders			
haematoma			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
hypertension			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
peripheral arterial occlusive disease			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
injection site pain			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
oedema			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
oedema peripheral			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 131 (1.53%)	0 / 130 (0.00%)	
occurrences (all)	2	0	
Reproductive system and breast disorders			

erectile dysfunction			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	1 / 130 (0.77%)	
occurrences (all)	1	1	
dyspnoea			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
epistaxis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
oropharyngeal pain			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
rhinitis allergic			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
burnout syndrome			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
depression			

alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 131 (1.53%)	0 / 130 (0.00%)	
occurrences (all)	2	0	
Investigations			
liver function test abnormal			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
contusion			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
joint sprain			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 131 (1.53%)	1 / 130 (0.77%)	
occurrences (all)	2	1	
thermal burn			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	1 / 130 (0.77%)	
occurrences (all)	1	1	
wound			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 131 (1.53%)	0 / 130 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			
supraventricular tachycardia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 131 (1.53%)	0 / 130 (0.00%)	
occurrences (all)	2	0	

migraine			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
polyneuropathy			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
ear pain			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
tinnitus			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 131 (1.53%)	0 / 130 (0.00%)	
occurrences (all)	2	0	
Eye disorders			
cataract			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
conjunctivitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
glaucoma			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

diarrhoea			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	2 / 130 (1.54%)	
occurrences (all)	1	2	
dyspepsia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
gastritis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
nausea			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
tooth disorder			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
toothache			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
vomiting			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	1 / 130 (0.77%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
dermatitis allergic			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
eczema			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
ingrowing nail			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
intertrigo			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
lipodystrophy acquired			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 131 (1.53%)	0 / 130 (0.00%)	
occurrences (all)	2	0	
lipohypertrophy			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
neuropathic ulcer			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
skin ulcer			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
cystitis noninfective			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
nephropathy			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
renal failure			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
renal impairment			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
arthritis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
back pain			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	3 / 131 (2.29%)	0 / 130 (0.00%)	
occurrences (all)	3	0	
joint effusion			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
muscle spasms			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
osteochondrosis			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
tendon pain			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
tenosynovitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
acute sinusitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
bronchitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	1 / 130 (0.77%)	
occurrences (all)	1	1	
cystitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 131 (1.53%)	0 / 130 (0.00%)	
occurrences (all)	2	0	
ear infection			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	2	
epstein-barr virus infection			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
fungal infection			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
gastroenteritis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	2 / 130 (1.54%)	
occurrences (all)	1	2	
infection			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
influenza			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	1 / 130 (0.77%)	
occurrences (all)	1	1	
nasopharyngitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	15 / 131 (11.45%)	12 / 130 (9.23%)	
occurrences (all)	18	13	
pneumonia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
pyelonephritis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
scarlet fever			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	0 / 130 (0.00%)	
occurrences (all)	1	0	
sinobronchitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	

tonsillitis			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	2 / 131 (1.53%)	1 / 130 (0.77%)	
occurrences (all)	2	1	
urinary tract infection			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	3 / 131 (2.29%)	2 / 130 (1.54%)	
occurrences (all)	3	2	
viral infection			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	1 / 130 (0.77%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
diabetic foot			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	2 / 130 (1.54%)	
occurrences (all)	1	2	
hypercholesterolaemia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	1 / 130 (0.77%)	
occurrences (all)	1	1	
hyperlipidaemia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	1 / 131 (0.76%)	1 / 130 (0.77%)	
occurrences (all)	1	1	
hypoglycaemia			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
iron deficiency			
alternative dictionary used: MedDRA 14.0			
subjects affected / exposed	0 / 131 (0.00%)	1 / 130 (0.77%)	
occurrences (all)	0	1	
obesity			
alternative dictionary used: MedDRA 14.0			

subjects affected / exposed occurrences (all)	0 / 131 (0.00%) 0	1 / 130 (0.77%) 1	

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