Clinical trial results:
Glycemic Control and Treatment Satisfaction Using Finesse Versus Pen for Initiating Bolus Insulin Dosing in Type 2 Diabetes Mellitus Subjects Not Achieving Glycemic Targets on Basal Insulin With/Without Anti-Hyperglycemic Agents

Summary

EudraCT number	2015-003761-28
Trial protocol	DE
Global end of trial date	31 August 2017

Results information

Result version number	v1 (current)
This version publication date	26 June 2022
First version publication date	26 June 2022

Trial information

Trial identification

Sponsor protocol code	VP-00525

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02542631
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Johnson & Johnson Diabetes Companies
Sponsor organisation address	965 Chesterbrook Boulevard, Wayne, Pennsylvania, United States, 19087
Public contact	Clinical Registry Group, Johnson & Johnson Diabetes Companies, clinicaltrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Johnson & Johnson Diabetes Companies, clinicaltrialsEU@its.jnj.com

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	31 August 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to compare Finesse to a Pen to initiate and maintain bolus insulin dosing assessed by comparing change in glycated hemoglobin (A1C) from Baseline to the completion of 24 weeks of basal and bolus insulin therapy on each treatment.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety was evaluated based on treatment-emergent adverse events, adverse device effect, serious adverse events, serious adverse device effect, hypoglycemic events, physical examination findings, vital signs, body weight, body mass index, clinical laboratory parameters (including serum chemistry, hematology, and urinalysis) and concomitant medication monitoring.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2015
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: 217
Country: Number of subjects enrolled	France: 33
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	United Kingdom: 22
Worldwide total number of subjects	278
EEA total number of subjects	39

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)	192
From 65 to 84 years	86
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 53 investigative sites in France, Germany, the United Kingdom, and the United States from 01 August 2015 to 31 August 2017.

Pre-assignment

Screening details:

A total of 388 subjects were screened, 110 subjects were screen failures mainly due to not meeting inclusion criteria and 278 subjects were randomised to receive study treatment.

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	Bolus Insulin Patch

Arm description:

Experimental Treatment Arm

Arm type	Experimental
Investigational medicinal product name	Bolus Insulin Patch
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal patch
Routes of administration	Transdermal use

Dosage and administration details:

Bolus insulin dosing with Finesse up to 24 months.

Arm title	Insulin Pen

Arm description:

Comparator Treatment Arm

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

Dosage and administration details:

Bolus insulin dosing with Pen device up to 24 months.

Number of subjects in period 1	Bolus Insulin Patch	Insulin Pen
Started	139	139
Completed	108	108
Not completed	31	31
Adverse event, serious fatal	1	2
Consent withdrawn by subject	11	16
Physician decision	6	4
Adverse event, non-fatal	1	1
Sponsor Termination	1	-
Used Prohibited Medication	2	1
Unspecified	2	1
Lost to follow-up	6	5
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Bolus Insulin Patch
Reporting group description: Experimental Treatment Arm	
Reporting group title	Insulin Pen
Reporting group description: Comparator Treatment Arm	

Reporting group values	Bolus Insulin Patch	Insulin Pen	Total
Number of subjects	139	139	278
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	58.1	60.4	
standard deviation	± 9.7	± 7.9	-
Sex: Female, Male Units:			
Female	58	52	110
Male	81	87	168
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	3	0	3
Native Hawaiian or Other Pacific Islander	4	1	5
Black or African American	12	11	23
White	120	126	246
More than one race	0	0	0
Unknown or Not Reported	0	0	0
A1C			
The intent-to-treat (ITT) analysis set consisted of all randomized subjects who initiated bolus insulin therapy.			
Units: A1C %			
arithmetic mean	8.6	8.7	
standard deviation	± 0.9	± 1.0	-

End points

End points reporting groups

Reporting group title	Bolus Insulin Patch
Reporting group description: Experimental Treatment Arm	
Reporting group title	Insulin Pen
Reporting group description: Comparator Treatment Arm	

Primary: Change in A1C from Baseline to the Completion of 24 Weeks of Basal and Bolus Insulin Therapy

End point title	Change in A1C from Baseline to the Completion of 24 Weeks of Basal and Bolus Insulin Therapy
End point description: The primary outcome measure analysis used a modified intent-to-treat (mITT) population data set which included all ITT subjects who had a baseline A1C and at least one post-baseline A1C measurement. For missing values, the last observation carried forward (LOCF) imputation method was used.	
End point type	Primary
End point timeframe: Baseline to Week 24	

End point values	Bolus Insulin Patch	Insulin Pen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	138		
Units: A1C %				
least squares mean (standard error)	-1.69 (± 0.08)	-1.60 (± 0.08)		

Statistical analyses

Statistical analysis title	Bolus Insulin Patch versus Insulin Pen
Comparison groups	Bolus Insulin Patch v Insulin Pen
Number of subjects included in analysis	274
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [1]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.14

Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[1] - Non-inferiority p-value was calculated with 2-sided comparison of the difference in treatment effects between Finesse and Pen with a non-inferiority margin of 0.4%.

Secondary: Number of Subjects with A1C less than or equal to (<=) 7.0 Percent (%) at Week 24

End point title	Number of Subjects with A1C less than or equal to (<=) 7.0 Percent (%) at Week 24

End point description:

Number of subjects with A1C <=7.0% at Week 24 were reported. The secondary outcome measure analysis used a mITT population data set which included all the ITT subjects who had a baseline A1C and at least one post-baseline A1C measurement. For missing values, the LOCF imputation method was used.

End point type	Secondary

End point timeframe:

24 weeks

End point values	Bolus Insulin Patch	Insulin Pen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	138		
Units: subjects	85	77		

Statistical analyses

Statistical analysis title	Bolus Insulin Patch versus Insulin Pen
Comparison groups	Bolus Insulin Patch v Insulin Pen
Number of subjects included in analysis	274
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.26 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	2.14
Variability estimate	Standard error of the mean
Dispersion value	0.25

Notes:

[2] - Statistical test of device effects was conducted at a 2-sided alpha level of 0.05, and confidence interval (CI) was calculated at 95%, 2-sided.

Secondary: Change in Percent of Glucose Values of Continuous Glucose Monitoring (CGM) Measurements Within Targeted Range of 71 and 180 mg/dl (4.0 and 10.0

mmol/l) From Baseline to Week 24

End point title	Change in Percent of Glucose Values of Continuous Glucose Monitoring (CGM) Measurements Within Targeted Range of 71 and 180 mg/dl (4.0 and 10.0 mmol/l) From Baseline to Week 24

End point description:

Change in percent of glucose values of CGM measurements within targeted range of 71 and 180 milligram per deciliter (mg/dl) (4.0 and 10.0 millimoles per liter [mmol/l]) from baseline to week 24 (in a subset of subjects) was reported. The CGM analysis set included all ITT subjects who had CGM measurements at a 1 to 2 week period of Week 2 to Week 0 and a 1 to 2 week period from Week 22 to Week 24.

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Bolus Insulin Patch	Insulin Pen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	49		
Units: Percent change				
least squares mean (standard error)	26.87 (± 2.33)	29.84 (± 2.40)		

Statistical analyses

Statistical analysis title	Bolus Insulin Patch versus Insulin Pen

Statistical analysis description:

ANCOVA model with treatment group as a factor and baseline value as a covariate was used to compare devices for continuous measures.

Comparison groups	Bolus Insulin Patch v Insulin Pen
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.38 [3]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.63
upper limit	3.7
Variability estimate	Standard error of the mean
Dispersion value	3.36

Notes:

[3] - Statistical test of device effects was conducted at a 2-sided alpha level of 0.05, and CI was calculated at 95%, 2-sided.

Secondary: Change in A1C from Baseline to Week 44

End point title	Change in A1C from Baseline to Week 44

End point description:

Change in A1C from baseline to the completion of 44 weeks of basal and bolus insulin therapy was reported. The secondary outcome measure analysis used a mITT population data set which included all the ITT subjects who had a baseline A1C and at least one post-baseline A1C measurement. For missing values, the LOCF imputation method was used.

End point type	Secondary

End point timeframe:

Baseline to Week 44

End point values	Bolus Insulin Patch	Insulin Pen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	109		
Units: A1C %				
least squares mean (standard error)	-1.63 (± 0.10)	-1.63 (± 0.10)		

Statistical analyses

Statistical analysis title	Bolus Insulin Patch versus Insulin Pen

Statistical analysis description:

ANCOVA model with treatment group as a factor and baseline value as a covariate was used to compare devices for continuous measures.

Comparison groups	Bolus Insulin Patch v Insulin Pen
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.99 [4]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[4] - Statistical test of device effects was conducted at a 2-sided alpha level of 0.05, and confidence interval (CI) was calculated at 95%, 2-sided.

Secondary: Number of Subjects with A1C <=7.0% at Week 44

End point title	Number of Subjects with A1C <=7.0% at Week 44

End point description:

Number of subjects with A1C <=7.0% after 44 weeks of basal and bolus insulin therapy were reported. The secondary outcome measure analysis used a mITT population data set which included all the ITT subjects who had a baseline A1C and at least one post-baseline A1C measurement. For missing values, the LOCF imputation method was used.

End point type	Secondary

End point timeframe:

Baseline to Week 44

End point values	Bolus Insulin Patch	Insulin Pen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	109		
Units: subjects	70	68		

Statistical analyses

Statistical analysis title	Bolus Insulin Patch versus Insulin Pen
Comparison groups	Bolus Insulin Patch v Insulin Pen
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.71 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.93
Variability estimate	Standard error of the mean
Dispersion value	0.28

Notes:

[5] - Statistical test of device effects was conducted at a 2-sided alpha level of 0.05, and confidence interval (CI) was calculated at 95%, 2-sided.

Secondary: Change in A1C from Week 24 to Week 44

End point title	Change in A1C from Week 24 to Week 44

End point description:

Change in A1C from week 24 to week 44 after basal and bolus insulin therapy were reported. The secondary outcome measure analysis used a mITT population data set which included all the ITT subjects who had a baseline A1C and at least one post-baseline A1C measurement. For missing values, the LOCF imputation method was used.

End point type	Secondary

End point timeframe:

Week 24 to Week 44

End point values	Bolus Insulin Patch	Insulin Pen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	109		
Units: A1C %				
least squares mean (standard error)	0.12 (± 0.06)	0.07 (± 0.06)		

Statistical analyses

Statistical analysis title	Bolus Insulin Patch versus Insulin Pen

Statistical analysis description:

ANCOVA model with treatment group as a factor and week 24 value as a covariate was used to compare devices for continuous measures.

Comparison groups	Bolus Insulin Patch v Insulin Pen
Number of subjects included in analysis	217
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.52 [6]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.24
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[6] - Statistical test of device effects was conducted at a 2-sided alpha level of 0.05, and confidence interval (CI) was calculated at 95%, 2-sided.

Secondary: Number of Subjects with Severe Hypoglycemic Event

End point title	Number of Subjects with Severe Hypoglycemic Event

End point description:

An event requiring the assistance of another person to actively administer carbohydrate (including intravenous dextrose), glucagon, or other resuscitative actions. Neurological recovery attributable to the restoration of plasma glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose concentration. The ITT analysis set consisted of all randomized subjects who initiated bolus insulin therapy.

End point type	Secondary

End point timeframe:

44 weeks

End point values	Bolus Insulin Patch	Insulin Pen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	139		
Units: subjects	3	3		

Statistical analyses

Statistical analysis title	Bolus Insulin Patch versus Insulin Pen
Comparison groups	Bolus Insulin Patch v Insulin Pen
Number of subjects included in analysis	278
Analysis specification	Pre-specified
Analysis type	
P-value	= 1
Method	Chi-squared

Other pre-specified: Change in Treatment Satisfaction from Baseline to Week 24

End point title	Change in Treatment Satisfaction from Baseline to Week 24

End point description:

Change in treatment satisfaction with insulin delivery system from baseline to week 24 was assessed by self-report on the validated Insulin Delivery System Rating Questionnaire. Scale is 0-100. Higher score is better. The other pre-specified outcome measure analysis used a mITT population data set which included all the ITT subjects who had a baseline A1C and at least one post-baseline A1C measurement. For missing values, the LOCF imputation method was used.

End point type	Other pre-specified

End point timeframe:

Baseline to Week 24

End point values	Bolus Insulin Patch	Insulin Pen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	117		
Units: units on a scale				
least squares mean (standard error)	13.63 (± 1.94)	4.47 (± 2.01)		

Statistical analyses

Statistical analysis title	Bolus Insulin Patch versus Insulin Pen

Statistical analysis description:

ANCOVA model with change in score as dependent variable, treatment as factor, and baseline score as a covariate was used to compare devices.

Comparison groups	Bolus Insulin Patch v Insulin Pen

Number of subjects included in analysis	241
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [7]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	9.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.65
upper limit	14.67
Variability estimate	Standard error of the mean
Dispersion value	2.8

Notes:

[7] - Statistical test of device effects was conducted at a 2-sided alpha level of 0.05, and confidence interval (CI) was calculated at 95%, 2-sided.

Other pre-specified: Change in Diabetes-specific Quality of Life from Baseline to Week 24

End point title	Change in Diabetes-specific Quality of Life from Baseline to Week 24

End point description:

Change in Diabetes-Specific Quality of Life (QOL), baseline to week 24 was assessed by self-report on the validated Diabetes Specific Quality of Life Survey. Scale is 0-100. Higher score is better. The pre-specified outcome measure analysis used a mITT population data set which included all the ITT subjects who had a baseline A1C and at least one post-baseline A1C measurement. For missing values, the LOCF imputation method was used.

End point type	Other pre-specified

End point timeframe:

Baseline to Week 24

End point values	Bolus Insulin Patch	Insulin Pen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	123		
Units: units on a scale				
least squares mean (standard error)	2.37 (± 1.43)	-1.95 (± 1.44)		

Statistical analyses

Statistical analysis title	Bolus Insulin Patch versus Insulin Pen

Statistical analysis description:

ANCOVA model with change in score as dependent variable, treatment as factor, and baseline score as a covariate was used to compare devices.

Comparison groups	Bolus Insulin Patch v Insulin Pen

Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03 [8]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	4.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	8.32
Variability estimate	Standard error of the mean
Dispersion value	2.03

Notes:

[8] - Statistical test of device effects was conducted at a 2-sided alpha level of 0.05, and confidence interval (CI) was calculated at 95%, 2-sided.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

44 weeks

Adverse event reporting additional description:

SAE: event that led to death; life-threatening illness or injury; impairment of body structure or function; in-patient or prolongation of hospitalisation; medical or surgical intervention to prevent life threatening illness or injury; impairment to body structure or function; or fetal distress or death; congenital abnormality; birth defect.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Insulin Pen

Reporting group description:

Comparator Treatment Arm

Reporting group title	Bolus Insulin Patch

Reporting group description:

Experimental Treatment Arm

Serious adverse events	Insulin Pen	Bolus Insulin Patch	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 139 (9.35%)	10 / 139 (7.19%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant, and unspecified			
subjects affected / exposed	2 / 139 (1.44%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	2 / 139 (1.44%)	2 / 139 (1.44%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Vascular disorders			

subjects affected / exposed	2 / 139 (1.44%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac disorders			
subjects affected / exposed	2 / 139 (1.44%)	5 / 139 (3.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 1	
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	2 / 139 (1.44%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General Disorders			
subjects affected / exposed	0 / 139 (0.00%)	2 / 139 (1.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Blood and lymphatic system disorders			
subjects affected / exposed	1 / 139 (0.72%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal disorders			
subjects affected / exposed	0 / 139 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infections and Infestations			
subjects affected / exposed	3 / 139 (2.16%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Metabolism and nutrition disorders			
subjects affected / exposed	1 / 139 (0.72%)	0 / 139 (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 Pen	Bolus Insulin Patch	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	99 / 139 (71.22%)	100 / 139 (71.94%)	
Investigations			
Investigations			
subjects affected / exposed	14 / 139 (10.07%)	10 / 139 (7.19%)	
occurrences (all)	14	10	
Vascular disorders			
Vascular disorders			
subjects affected / exposed	8 / 139 (5.76%)	12 / 139 (8.63%)	
occurrences (all)	9	12	
Nervous system disorders			
Nervous system disorders			
subjects affected / exposed	16 / 139 (11.51%)	13 / 139 (9.35%)	
occurrences (all)	19	15	
General disorders and administration site conditions			
General disorders			
subjects affected / exposed	15 / 139 (10.79%)	28 / 139 (20.14%)	
occurrences (all)	15	39	
Gastrointestinal disorders			
Gastrointestinal disorders			
subjects affected / exposed	21 / 139 (15.11%)	23 / 139 (16.55%)	
occurrences (all)	31	37	
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic, and mediastinal disorders			
subjects affected / exposed	17 / 139 (12.23%)	14 / 139 (10.07%)	
occurrences (all)	22	18	
Musculoskeletal and connective tissue disorders			

Musculoskeletal and connective tissue			
subjects affected / exposed	32 / 139 (23.02%)	34 / 139 (24.46%)	
occurrences (all)	42	48	
Infections and infestations			
Infections and infestations			
subjects affected / exposed	60 / 139 (43.17%)	51 / 139 (36.69%)	
occurrences (all)	85	84	

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