Clinical trial results:
A phase IV, randomized, double blind cross-over study to evaluate palatability of Patiromer compared to Sodium Polystyrene Sulfonate in healthy subjects

Summary

EudraCT number	2019-004696-40
Trial protocol	FR
Global end of trial date	03 September 2020

Results information

Result version number	v1 (current)
This version publication date	18 September 2021
First version publication date	18 September 2021

Trial information

Trial identification

Sponsor protocol code	PAT-PAL-404

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Vifor (International), Inc.
Sponsor organisation address	Rechenstrasse 37, St. Gallen,, Switzerland, 9014
Public contact	PAT-PAL-404 Clinical Study Team, Vifor (International), Inc., +41 588 518 000, PAT-PAL-404.study@viforpharma.com
Scientific contact	PAT-PAL-404 Clinical Study Team, Vifor (International), Inc., +41 588 518 000, PAT-PAL-404.study@viforpharma.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	14 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 September 2020
Global end of trial reached?	Yes
Global end of trial date	03 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective:
- Compare the overall acceptability of patiromer with sodium polystyrene sulfonate (SPS).

Secondary Objectives:
- Determine factors for non-positive acceptability (non-liking)
- Determine the willingness for long-term use of patiromer and SPS

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki including amendments in force up to and including the time the study was conducted.

The study was conducted in compliance with the International Council for Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP), Committee for Proprietary Medicinal Products Guideline (CPMP/ICH/135/95), compliant with the EU Clinical Trial Directive (Directive 2001/20/EC).

Prior to initiation of the study, the protocol, the subject information sheet, and the Informed Consent Form (ICF) were reviewed and approved by an Independent Ethics Committee (IEC), CPP OUEST II – Angers, France, operating in accord with current regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 March 2020
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	France: 68
Worldwide total number of subjects	68
EEA total number of subjects	68

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)	55
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

From a total of 98 subjects screened 30 subjects were not included due to the following reasons: screen failrues (23 subjects); consent removal (5 subjects); supplementary subjects (2 subjects). A total of 68 of these subjects were included and randomised in the study. All subjects completed the study as per protocol.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Test-Reference

Arm description:

Subjects assigned to treatment-sequence group T-R (T=test treatment and R=reference treatment) receiving Patiromer on Day 1 and Sodium Polystyrene Sulfonate on Day 2.

Arm type	Experimental
Investigational medicinal product name	Patiromer
Investigational medicinal product code	
Other name	Veltassa®
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Single dose of 8.4 g reconstituted with 80 ml of water before use and administrated latest 3 hours after breakfast. The administration was on D1 or D2 according to the randomisation.

Investigational medicinal product name	Sodium polystyrene sulfonate
Investigational medicinal product code	
Other name	Kayexalate®
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Single dose of 15 g reconstituted with 80 ml of water before use and administrated latest 3 hours after breakfast. The administration was on D1 or D2 according to the randomisation.

Arm title	Reference-Test

Arm description:

Subjects assigned to treatment-sequence group R-T (R=reference treatment and T=test treatment) receiving Sodium Polystyrene Sulfonate on Day 1 and Patiromer on Day 2.

Arm type	Experimental
Investigational medicinal product name	Sodium Polystyrene Sulfonate
Investigational medicinal product code	
Other name	Kayexalate®
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Single dose of 15 g reconstituted with 80 ml of water before use and administrated latest 3 hours after breakfast. The administration was on D1 or D2 according to the randomisation.

Investigational medicinal product name	Patiromer
Investigational medicinal product code	
Other name	Veltassa®
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Single dose of 8.4 g reconstituted with 80 ml of water before use and administrated latest 3 hours after breakfast. The administration was on D1 or D2 according to the randomisation.

Number of subjects in period 1	Test-Reference	Reference-Test
Started	34	34
Completed	34	34

Baseline characteristics

Reporting groups	
Reporting group title	Test-Reference

Reporting group description:

Subjects assigned to treatment-sequence group T-R (T=test treatment and R=reference treatment) receiving Patiromer on Day 1 and Sodium Polystyrene Sulfonate on Day 2.

Reporting group title	Reference-Test

Reporting group description:

Subjects assigned to treatment-sequence group R-T (R=reference treatment and T=test treatment) receiving Sodium Polystyrene Sulfonate on Day 1 and Patiromer on Day 2.

Reporting group values	Test-Reference	Reference-Test	Total
Number of subjects	34	34	68
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	47.7	45.9	
standard deviation	± 14.9	± 15.6	-
Gender categorical			
Units: Subjects			
Female	19	18	37
Male	15	16	31

Subject analysis sets	
Subject analysis set title	Patiromer
Subject analysis set type	Full analysis

Subject analysis set description:

All 68 subjects included in the study were randomised (Sequence T-R, N=34; Sequence R-T; N=34) and received both test and reference but alternatively. All 68 subjects were included in all analysis populations (intent-to-treat set (ITTS)/per-protocol set (PPS)/safety set (SS), N=68).

Subject analysis set title	Sodium polystyrene sulfonate
Subject analysis set type	Full analysis

Subject analysis set description:

All 68 subjects included in the study were randomised (Sequence T-R, N=34; Sequence R-T; N=34) and received both test and reference but alternatively. All 68 subjects were included in all analysis populations (intent-to-treat set (ITTS)/per-protocol set (PPS)/safety set (SS), N=68).

Reporting group values	Patiromer	Sodium polystyrene sulfonate	
Number of subjects	68	68	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	46.8	46.8	

standard deviation	± 15.2	± 15.2	

Gender categorical Units: Subjects			
Female	37	37	
Male	31	31	

End points

End points reporting groups

Reporting group title	Test-Reference

Reporting group description:

Subjects assigned to treatment-sequence group T-R (T=test treatment and R=reference treatment) receiving Patiromer on Day 1 and Sodium Polystyrene Sulfonate on Day 2.

Reporting group title	Reference-Test

Reporting group description:

Subjects assigned to treatment-sequence group R-T (R=reference treatment and T=test treatment) receiving Sodium Polystyrene Sulfonate on Day 1 and Patiromer on Day 2.

Subject analysis set title	Patiromer
Subject analysis set type	Full analysis

Subject analysis set description:

All 68 subjects included in the study were randomised (Sequence T-R, N=34; Sequence R-T; N=34) and received both test and reference but alternatively. All 68 subjects were included in all analysis populations (intent-to-treat set (ITTS)/per-protocol set (PPS)/safety set (SS), N=68).

Subject analysis set title	Sodium polystyrene sulfonate
Subject analysis set type	Full analysis

Subject analysis set description:

All 68 subjects included in the study were randomised (Sequence T-R, N=34; Sequence R-T; N=34) and received both test and reference but alternatively. All 68 subjects were included in all analysis populations (intent-to-treat set (ITTS)/per-protocol set (PPS)/safety set (SS), N=68).

Primary: Overall Acceptability Score

End point title	Overall Acceptability Score

End point description:

LSM= Least squares means SPS= sodium polystyrene sulfonate

A 9-point hedonic score (Palability questionnaire) was used to compare the overall acceptability of patiromer with SPS. The levels of rating ranged from 1 dislike extremely, 2 dislike very much, 3 dislike moderately, 4 dislike slightly, 5 neither like nor dislike, 6 like slightly, 7 like moderately, 8 like very much, to 9 like extremely.

The overall acceptability score was analysed using a linear mixed model, including study treatment (test/reference, sequence, sex, age, BMI) and interaction terms as fixed effects (i.e., 15 variables). A selection of variables was performed by backward elimination.

End point type	Primary

End point timeframe:

overall study period

End point values	Patiromer	Sodium polystyrene sulfonate		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	68		
Units: Hedonic Score				
least squares mean (standard error)				
LSM for each treatment group	5.426 (± 0.206)	5.000 (± 0.206)		

Statistical analyses

Statistical analysis title	Overall acceptability - Patiromer

Statistical analysis description:

Subjects in this analysis n=136 refers to the sum of subjects treated with each treatment (N=68 for Patiromer; N=68 for SPS).

Comparison groups	Patiromer v Sodium polystyrene sulfonate
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0968 [1]
Method	Linear mixed model
Parameter estimate	Mean difference (final values)
Point estimate	-0.426
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.932
upper limit	0.0791
Variability estimate	Standard error of the mean
Dispersion value	0.253

Notes:

[1] - No significant difference between treatment groups was detected (p=0.0968).

Secondary: Positive Acceptability (Liking)

End point title	Positive Acceptability (Liking)

End point description:

Number of subjects with positive ratings for overall acceptability, mixing appearance, smell, taste, mouth feel/texture/consistency and aftertaste: Positive rating includes scores from 6 ("like slightly") to 9 ("like extremely").

End point type	Secondary

End point timeframe:

overall study period

End point values	Patiromer	Sodium polystyrene sulfonate		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	68		
Units: Number of subjects				
number (not applicable)				
Overall acceptability - Yes	32	25		

Overall accetability - No	36	43		
Mixing - Yes	30	45		
Mixing - No	38	23		
Appearance - Yes	38	37		
Appearance - No	30	31		
Smell - Yes	24	40		
Smell - No	44	28		
Taste - Yes	19	22		
Taste - No	49	46		
Feel/texture/consistency - Yes	17	13		
Feel/texture/consistency - No	51	55		
Swallowing - Yes	32	20		
Swallowing - No	36	48		
Aftertaste - Yes	22	19		
Aftertaste - No	46	49		

Statistical analyses

Statistical analysis title	LR positive overall acceptability

Statistical analysis description:

LR = logistic regression

Subjects in this analysis n=136 refers to the sum of subjects treated with each treatment (N=68 for Patiromer; N=68 for SPS).Descriptive statistics showed that the proportion of subjects with positive ratings (rating ≥6) for the overall acceptability was higher in the patiromer group (47%) as compared to the SPS group (37%).

Comparison groups	Patiromer v Sodium polystyrene sulfonate
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1753 [2]
Method	Regression, Logistic
Parameter estimate	logistic regression
Point estimate	-0.4245
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.0385
upper limit	0.1894
Variability estimate	Standard error of the mean
Dispersion value	0.3132

Notes:

[2] - The difference was not statistically significant (p=0.1753).

Secondary: Non-Positive Acceptability (Non-Liking)

End point title	Non-Positive Acceptability (Non-Liking)

End point description:

Number of subjects with negative ratings for overall acceptability was evaluated: negative rating includes scores from 4 (“dislike slightly”) to 1 (“dislike extremely”).

End point type	Secondary

End point timeframe:
overall study period

End point values	Patiromer	Sodium polystyrene sulfonate		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	68		
Units: Number of subjects				
number (not applicable)				
Overall acceptability - Yes	19	32		
Overall acceptability - No	49	36		
Mixing - Yes	24	10		
Mixing - No	44	58		
Appearance - Yes	18	18		
Appearance - No	50	50		
Smell - Yes	3	7		
Smell - No	65	61		
Taste - Yes	11	27		
Taste - No	57	41		
Texture - Yes	35	47		
Texture - No	33	21		
Swallowing - Yes	20	28		
Swallowing - No	48	40		
Aftertaste - Yes	16	32		
Aftertaste - No	52	36		

Statistical analyses

Statistical analysis title	LR non-positive overall acceptability

Statistical analysis description:
LR = logistic regression

Subjects in this analysis n=136 refers to the sum of subjects treated with each treatment (N=68 for Patiromer; N=68 for SPS). Descriptive statistics showed that the proportion of subjects with negative ratings for overall acceptability was higher in the SPS group (47%) as compared to the patiromer group (28%).

Comparison groups	Patiromer v Sodium polystyrene sulfonate
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0195 [3]
Method	Regression, Logistic
Parameter estimate	logistic regression
Point estimate	0.9286

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1495
upper limit	1.7077
Variability estimate	Standard error of the mean
Dispersion value	0.3975

Notes:

[3] - A significant treatment effect was confirmed by logistic regression (p=0.0195).

Secondary: Description of Acceptability Sub-scores

End point title	Description of Acceptability Sub-scores

End point description:

Determination of factors of non-positive palatability rating based on the scores from 4 ("dislike slightly") to 1 ("dislike extremely). In case of non-liking of taste, texture, swallowing, aftertaste, the subjects were asked for the reasons of non-liking by offering pre-defined options to select from including free text description.

End point type	Secondary

End point timeframe:

overall study period

End point values	Patiromer	Sodium polystyrene sulfonate		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	68		
Units: Number of subjects				
number (not applicable)				
Problem taste – Too salty	0	3		
Problem taste – Too bitter	4	5		
Problem taste – Too sour/acidic	0	2		
Problem taste – Too sweet	0	1		
Problem taste – Too astringent	5	12		
Problem taste – Other reasons	2	4		
Problem taste – No problem	57	41		
Problem texture – Too grainy/sandy	24	25		
Problem texture – Too sticky	1	1		
Problem texture – Too thick/heavy	5	8		
Problem texture – Too lingering	4	9		
Problem texture – Other reasons	1	4		
Problem texture - No problem	33	21		
Problem swallowing – Too thick/heavy	3	8		
Problem swallowing – Too fuzzy	12	8		
Problem swallowing – Too difficult/strenuous	3	8		
Problem swallowing – Other reasons	2	4		
Problem swallowing – No problem	48	40		
Problem aftertaste – Too grainy/sandy	9	11		
Problem aftertaste – Too sticky	3	3		
Problem aftertaste – Too lingering	2	4		

Problem aftertaste - No problem	54	50		

Statistical analyses

Statistical analysis title	LMM on acceptability - Mixing

Statistical analysis description:

LMM = Linear mixed model
Linear mixed model on acceptability sub-score for mixing

Subjects in this analysis n=136 refers to the sum of subjects treated with each treatment (N=68 for Patiromer; N=68 for SPS).

Comparison groups	Patiromer v Sodium polystyrene sulfonate
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002 [4]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.015
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4926
upper limit	1.5368
Variability estimate	Standard error of the mean
Dispersion value	0.261

Notes:

[4] - A statistically significant difference between treatments in favour of SPS for the mixing sub-score (p=0.0002) was shown.

Statistical analysis title	LMM on acceptability - Feel/texture/consistency

Statistical analysis description:

LMM = Linear mixed model
Linear mixed model on acceptability sub-score for feel/texture/consistency

Subjects in this analysis n=136 refers to the sum of subjects treated with each treatment (N=68 for Patiromer; N=68 for SPS).

Comparison groups	Sodium polystyrene sulfonate v Patiromer
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0195 [5]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.618
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1326
upper limit	-0.1027

Variability estimate	Standard error of the mean
Dispersion value	0.258

Notes:

[5] - A statistically significant difference between treatments in favour of patiromer for the feel/texture/consistency sub-score (p=0.0195) was shown.

Statistical analysis title	LMM on acceptability - Swallowing

Statistical analysis description:

LMM = Linear mixed model
Linear mixed model on acceptability sub-score for swallowing

Subjects in this analysis n=136 refers to the sum of subjects treated with each treatment (N=68 for Patiromer; N=68 for SPS).

Comparison groups	Patiromer v Sodium polystyrene sulfonate
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0048 [6]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.618
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.0401
upper limit	-0.1952
Variability estimate	Standard error of the mean
Dispersion value	0.212

Notes:

[6] - A statistically significant difference between treatments in favour of patiromer for the swallowing sub-score (p=0.0048) was shown.

Statistical analysis title	LMM on acceptability - Aftertaste

Statistical analysis description:

LMM = Linear mixed model
Linear mixed model on acceptability sub-score for aftertaste

Subjects in this analysis n=136 refers to the sum of subjects treated with each treatment (N=68 for Patiromer; N=68 for SPS).

Comparison groups	Patiromer v Sodium polystyrene sulfonate
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0162 [7]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.676
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.224
upper limit	-0.1289
Variability estimate	Standard error of the mean
Dispersion value	0.274

Notes:

[7] - A statistically significant difference between treatments in favour of patiromer for the aftertaste sub-score (p=0.0162) was shown.

Other pre-specified: Willingness for long term use

End point title	Willingness for long term use

End point description:

Willingness to take the medicinal product every day for 3 months, 6 months, 12 months or longer than 12 months.

End point type	Other pre-specified

End point timeframe:

overall study period

End point values	Patiromer	Sodium polystyrene sulfonate		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	68		
Units: Number of subjects				
number (not applicable)				
3 months	34	34		
6 months	44	24		
12 months	43	25		
Longer than 12 months	44	24		

Statistical analyses

Statistical analysis title	6 months - Binomial Exact Test

Statistical analysis description:

The willingness for long-term use of patiromer and SPS was analysed by descriptive statistics and a test of compatibility of data with a binomial (equal weight) distribution between patiromer and SPS.

Comparison groups	Patiromer v Sodium polystyrene sulfonate
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0205 [8]
Method	Binomial Exact Test

Notes:

[8] - The subjects were statistically more willing to use patiromer versus SPS from 6 months onwards: 6 months (64.7% versus 35.3%, p-value=0.0205)

Statistical analysis title	12 months - Binomial Exact Test

Statistical analysis description:

The willingness for long-term use of patiromer and SPS was analysed by descriptive statistics and a test of compatibility of data with a binomial (equal weight) distribution between patiromer and SPS.

Comparison groups	Patiromer v Sodium polystyrene sulfonate

Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0385 [9]
Method	Binomial Exact Test

Notes:

[9] - The subjects were statistically more willing to use patiromer versus SPS from 6 months onwards: 12 months (63.2% versus 36.8%, p-value=0.0385)

Statistical analysis title	More than 12 months - Binomial Exact Test

Statistical analysis description:

The willingness for long-term use of patiromer and SPS was analysed by descriptive statistics and a test of compatibility of data with a binomial (equal weight) distribution between patiromer and SPS.

Comparison groups	Patiromer v Sodium polystyrene sulfonate
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0205 [10]
Method	Binomial Exact Test

Notes:

[10] - The subjects were statistically more willing to use patiromer versus SPS from 6 months onwards: More than 12 months (64.7% versus 35.3, p-value=0.0205)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

overall study period

Adverse event reporting additional description:

All the TEAEs were of mild to moderate intensity.
All the TEAEs were resolved before the end of the study.
No SAEs were reported during this study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Patiromer

Reporting group description:

All 68 subjects included in the study were randomised (Sequence T-R, N=34; Sequence R-T; N=34) and received both test and reference but alternatively. All 68 subjects were included in all analysis populations (intent-to-treat set (ITTS)/per-protocol set (PPS)/safety set (SS), N=68).

Reporting group title	Sodium polystyrene sulfonate

Reporting group description:

All 68 subjects included in the study were randomised (Sequence T-R, N=34; Sequence R-T; N=34) and received both test and reference but alternatively. All 68 subjects were included in all analysis populations (intent-to-treat set (ITTS)/per-protocol set (PPS)/safety set (SS), N=68).

Serious adverse events	Patiromer	Sodium polystyrene sulfonate	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 68 (0.00%)	0 / 68 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Patiromer	Sodium polystyrene sulfonate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 68 (8.82%)	3 / 68 (4.41%)	
Nervous system disorders			
Dizziness postural			
subjects affected / exposed	0 / 68 (0.00%)	1 / 68 (1.47%)	
occurrences (all)	0	1	
Headache			

subjects affected / exposed	3 / 68 (4.41%)	2 / 68 (2.94%)	
occurrences (all)	3	2	
Paraesthesia			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences (all)	1	0	
Sciatica			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 68 (1.47%)	0 / 68 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 September 2020	Implementation of health measures related to the COVID pandemic.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported