Clinical trial results:
A Phase 4, Multicenter Study to Evaluate Discontinuation and Re-Treatment in Subjects With Tenosynovial Giant Cell Tumor (TGCT) Previously Treated With Pexidartinib

Summary

EudraCT number	2020-000192-20
Trial protocol	HU NL IT
Global end of trial date	07 July 2023

Results information

Result version number	v1 (current)
This version publication date	27 October 2024
First version publication date	27 October 2024

Trial information

Trial identification

Sponsor protocol code	PL3397-A-U4003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04526704
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Daiichi Sankyo, Inc.
Sponsor organisation address	211 Mount Airy Road, Basking Ridge, United States, 07920
Public contact	Contact for Clinical Trial Information, Daiichi Sankyo, Inc., +1 908-992-6400, CTRinfo@dsi.com
Scientific contact	Contact for Clinical Trial Information, Daiichi Sankyo, Inc., +1 908-992-6400, CTRinfo@dsi.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	07 July 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to determine the proportion of patients who remained treatment-free. Secondary objectives in the Treatment-free Period was change from baseline in PROs and safety and in the Re-Treatment Period it was change from baseline in PROs, tumor assessment , and safety.

Protection of trial subjects:

The study was conducted in compliance with ethical principles that have their origin in the Declarations of Helsinki and in accordance with guidelines. The study protocol, amendments, the informed consent/assent form(s), and information sheets were approved by the appropriate and applicable Independent Ethics Committees (IECs) or Institutional Review Boards (IRBs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 October 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	Hungary: 2
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	32
EEA total number of subjects	16

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	28
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 32 participants who met all inclusion criteria and no exclusion criteria were enrolled in the study.

Pre-assignment

Screening details:

As specified in the protocol, the study analysis was conducted based on 2 cohorts: Treatment Continuation Cohort and Treatment-Free/Re-Treatment Cohort. Patient disposition, efficacy and safety endpoints were assessed based on these 2 cohorts, not according to the sequential nature of the arm/group assignment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Treatment Continuation Cohort

Arm description:

Previously-treated participants with TGCT who continued their current dose of pexidartinib treatment.

Arm type	Experimental
Investigational medicinal product name	Pexidartinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

200 mg capsules administered orally twice daily on an empty stomach (at least 1 hour before or at least 2 hours after a meal or snack)

Arm title	Treatment-Free/Re-Treatment Cohort

Arm description:

Previously-treated participants with TGCT who discontinued pexidartinib treatment (Treatment-Free Period) and had the option to resume pexidartinib treatment at dose of completion of prior study (Re-Treatment Period).

Arm type	Experimental
Investigational medicinal product name	Pexidartinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

200 mg capsules administered orally twice daily on an empty stomach (at least 1 hour before or at least 2 hours after a meal or snack)

Number of subjects in period 1	Treatment Continuation Cohort	Treatment-Free/Re-Treatment Cohort
Started	21	11
Completed	17	11
Not completed	4	0
Physician decision	1	-
Consent withdrawn by subject	2	-
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Continuation Cohort
Reporting group description:	
Previously-treated participants with TGCT who continued their current dose of pexidartinib treatment.	
Reporting group title	Treatment-Free/Re-Treatment Cohort
Reporting group description:	
Previously-treated participants with TGCT who discontinued pexidartinib treatment (Treatment-Free Period) and had the option to resume pexidartinib treatment at dose of completion of prior study (Re-Treatment Period).	

Reporting group values	Treatment Continuation Cohort	Treatment-Free/Re-Treatment Cohort	Total
Number of subjects	21	11	32
Age categorical Units: participants			
18 to 40 years	7	1	8
41 to 64 years	12	8	20
65 to 74 years	1	1	2
75 to 84 years	1	1	2
≥ 85 years	0	0	0
Age continuous Units: years			
arithmetic mean	46.2	51.9	
standard deviation	± 15.7	± 15.2	-
Gender categorical Units: Subjects			
Female	12	4	16
Male	9	7	16
Race/Ethnicity, Customized Units: Subjects			
Asian	1	1	2
White	19	8	27
Not collected per local regulations	1	2	3

End points

End points reporting groups

Reporting group title	Treatment Continuation Cohort
Reporting group description:	
Previously-treated participants with TGCT who continued their current dose of pexidartinib treatment.	
Reporting group title	Treatment-Free/Re-Treatment Cohort
Reporting group description:	
Previously-treated participants with TGCT who discontinued pexidartinib treatment (Treatment-Free Period) and had the option to resume pexidartinib treatment at dose of completion of prior study (Re-Treatment Period).	

Primary: Number of Treatment-Free Participants at 12 Months In The Treatment-free/Re-treatment Cohort

End point title	Number of Treatment-Free Participants at 12 Months In The Treatment-free/Re-treatment Cohort[1][2]
End point description:	
Participants who were not remaining treatment-free were defined as either participants who resumed pexidartinib treatment, death (any cause) or who were receiving systemic therapy or undergoing surgery for the treatment of TGCT, whichever occurs first. The number of participants who remained treatment-free at Month 12 is reported.	
End point type	Primary
End point timeframe:	
Baseline up to 12 months after last participant enrolled in Cohort	

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: Descriptive statistics were used to assess this outcome.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics were used to assess this outcome.

End point values	Treatment-Free/Re-Treatment Cohort			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: participants	8			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Treatment-Free Participants at 24 Months In The Treatment-free/Re-treatment Cohort

End point title	Number of Treatment-Free Participants at 24 Months In The Treatment-free/Re-treatment Cohort[3][4]
End point description:	
Participants who were not remaining treatment-free were defined as either participants who resumed	

pexidartinib treatment, death (any cause) or who were receiving systemic therapy or undergoing surgery for the treatment of TGCT, whichever occurs first. The number of participants who remained treatment-free at Month 24 is reported.

End point type	Primary

End point timeframe:

Baseline up to 24 months after last participant enrolled in Cohort

Notes:

[3] - 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: Descriptive statistics were used to assess this outcome.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics were used to assess this outcome.

End point values	Treatment-Free/Re-Treatment Cohort			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: participants	8			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PROMIS Physical Function Total Overall Score In The Treatment Continuation and Treatment-free/Re-Treatment Cohorts

End point title	Change From Baseline in PROMIS Physical Function Total Overall Score In The Treatment Continuation and Treatment-free/Re-Treatment Cohorts

End point description:

The PROMIS Physical Function Total Overall Score (includes 11 upper extremity questions and 13 lower extremity questions) ranges from 24 to 120, with each individual question being rated on a 5-point rating scale (where 1 is unable to do and 5 is without any difficulty). Higher PROMIS Physical Function Total Overall Scores indicate a better health state. The change from baseline in PROMIS Physical Function Total Overall Scores is being reported.

End point type	Secondary

End point timeframe:

Baseline up to Month 24

End point values	Treatment Continuation Cohort	Treatment-Free/Re-Treatment Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	7		
Units: score on a scale				
arithmetic mean (standard deviation)	-2.78 (± 6.42)	-1.93 (± 4.80)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EQ-5D-5L Scale Score In The Treatment Continuation and Treatment-free/Re-Treatment Cohorts

End point title	Change From Baseline in EQ-5D-5L Scale Score In The Treatment Continuation and Treatment-free/Re-Treatment Cohorts

End point description:

The EQ-5D-5L questionnaire assessed a participant's mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The overall health is rated on a scale from 0 to 100, where 0 is worst health you can imagine and 100 is best health you can imagine. The change from baseline in EQ-5D-5L Scale Score is being reported.

End point type	Secondary

End point timeframe:

Baseline up to Month 24

End point values	Treatment Continuation Cohort	Treatment-Free/Re-Treatment Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	7		
Units: score on a scale				
arithmetic mean (standard deviation)	-2.4 (± 13.53)	3.4 (± 7.59)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Reported Treatment-Emergent Adverse Events (TEAEs) In The Treatment Continuation Cohort

End point title	Number of Participants Who Reported Treatment-Emergent Adverse Events (TEAEs) In The Treatment Continuation Cohort[5]

End point description:

Treatment-emergent adverse events (TEAEs) were defined as new adverse events (AEs) or pre-existing conditions that worsen in CTCAE grade after the first dose of study drug and up to 30 days after last dose of study drug.

End point type	Secondary

End point timeframe:

Baseline up to 30 days after the start of re-treatment or end of study (whichever occurs first), up to 24 months

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics were used to assess this outcome.

End point values	Treatment Continuation Cohort			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: participants				
TEAE	19			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With and Without Progressive Disease

End point title	Number of Participants With and Without Progressive Disease

End point description:

Tumors were assessed based on the RECIST criteria. CR was defined as a disappearance of all target lesions, PR was defined as at least a 30% decrease in the sum of diameters of target lesions, and stable disease (SD) was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD; ≥30% increase in volume relative to lowest score during the study whether at baseline or some other visit.

End point type	Secondary

End point timeframe:

Month 18 (Re-treatment Period of the Treatment-free/Re-treatment Cohort), Month 24 (Treatment Continuation Cohort)

End point values	Treatment Continuation Cohort	Treatment-Free/Re-Treatment Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	3		
Units: participants				
Not progressive	16	0		
Progressive disease	0	1		
Not evaluable	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Reported Treatment-Emergent Adverse Events (TEAEs) In The Re-Treatment Period of the Treatment-free/Re-Treatment

Cohort	
End point title	Number of Participants Who Reported Treatment-Emergent Adverse Events (TEAEs) In The Re-Treatment Period of the Treatment-free/Re-Treatment Cohort[6]

End point description:

Treatment-emergent adverse events (TEAEs) were defined as new adverse events (AEs) or pre-existing conditions that worsen in CTCAE grade after the first dose of study drug and up to 30 days after last dose of study drug.

End point type	Secondary

End point timeframe:

Baseline up to 30 days after the start of re-treatment or end of study (whichever occurs first), up to 24 months

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics were used to assess this outcome.

End point values	Treatment-Free/Re-Treatment Cohort			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: participants				
TEAE	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients Reporting AEs (Treatment-free)

End point title	Number of Patients Reporting AEs (Treatment-free) [7]

End point description:

Adverse events (AEs) were defined as any untoward medical occurrence in a participant who was administered a pharmaceutical product and that does not necessarily have to have a causal relationship with this treatment.

End point type	Secondary

End point timeframe:

Baseline up to 30 days after the start of re-treatment or end of study (whichever occurs first), up to 24 months

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive statistics were used to assess this outcome.

End point values	Treatment-Free/Re-Treatment Cohort			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: participants				
Any Grade AE	7			

Any Grade Musculoskeletal/Tissue Disorders	6			
Any Grade Arthralgia	2			
Any Grade Back pain	2			
Any Grade Intervertebral disc protrusion	1			
Any Grade Joint swelling	1			
Any Grade Musculoskeletal pain	1			
Any Grade Pain in extremity	1			
Any Grade Metabolism and Nutrition Disorders	3			
Any Grade Hypercholesterolaemia	2			
Any Grade Hypertriglyceridaemia	2			
Any Grade General Disorders & Site Conditions	2			
Any Grade Asthenia	1			
Any Grade Oedema peripheral	1			
Any Grade Infections and Infestations	2			
Any Grade Cellulitis	1			
Any Grade COVID-19	1			
Any Grade investigations	2			
Any Gr Blood creatinine phosphokinase increased	2			
Any Grade Blood uric acid increased	1			
Any Renal and Urinary Disorders	2			
Any Renal colic	1			
Any Grade Urinary retention	1			
Any Grade Injury, Poisoning & Procedural Issues	1			
Any Grade Animal bite	1			
Any Grade Neoplasms Benign, Malignant & Other	1			
Any Grade Lipoma	1			
Any Grade Nervous System Disorders	1			
Any Grade Sciatica	1			
Any Grade Skin and Subcutaneous Tissue Disorders	1			
Any Grade Urticaria	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events were collected from baseline up to 30 days after the start of re-treatment or end of study (whichever occurs first), up to 24 months.

Adverse event reporting additional description:

TEAEs observed in the Treatment Continuation Cohort and the Re-Treatment Period of the Treatment-free/Re-Treatment Cohort are reported. AEs from the Treatment-free Period of the Treatment-free/Re-Treatment Cohort were captured and are reported as well.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26

Reporting groups

Reporting group title	Treatment Continuation Cohort

Reporting group description:

Previously-treated participants with TGCT who continued their current dose of pexidartinib treatment.

Reporting group title	Re-Treatment Period of Treatment- Free/Re-Treatment Cohort

Reporting group description:

Previously-treated participants with TGCT who discontinued pexidartinib treatment (Treatment-Free Period) and had the option to resume pexidartinib treatment at dose of completion of prior study (Re-Treatment Period).

Reporting group title	Treatment-Free Period of Treatment- Free/Re-treatment Cohort

Reporting group description:

Previously-treated participants with TGCT who discontinued pexidartinib treatment (Treatment-Free Period) and reported adverse events.

Serious adverse events	Treatment Continuation Cohort	Re-Treatment Period of Treatment-Free/Re-Treatment Cohort	Treatment-Free Period of Treatment-Free/Re-treatment Cohort
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 21 (9.52%)	0 / 3 (0.00%)	0 / 11 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Product issues			
Device dislocation			
subjects affected / exposed	1 / 21 (4.76%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Creutzfeldt-Jakob disease			

subjects affected / exposed	1 / 21 (4.76%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Treatment Continuation Cohort	Re-Treatment Period of Treatment-Free/Re-Treatment Cohort	Treatment-Free Period of Treatment-Free/Re-treatment Cohort
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 21 (90.48%)	3 / 3 (100.00%)	7 / 11 (63.64%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 21 (9.52%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 21 (14.29%)	1 / 3 (33.33%)	1 / 11 (9.09%)
occurrences (all)	3	1	1
Fatigue			
subjects affected / exposed	3 / 21 (14.29%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Generalised oedema			
subjects affected / exposed	0 / 21 (0.00%)	1 / 3 (33.33%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 21 (9.52%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 21 (9.52%)	1 / 3 (33.33%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 21 (23.81%)	1 / 3 (33.33%)	0 / 11 (0.00%)
occurrences (all)	5	1	0
Blood creatinine phosphokinase increased			
subjects affected / exposed	8 / 21 (38.10%)	2 / 3 (66.67%)	2 / 11 (18.18%)
occurrences (all)	8	2	2
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 21 (4.76%)	1 / 3 (33.33%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 21 (4.76%)	1 / 3 (33.33%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 21 (0.00%)	1 / 3 (33.33%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
White blood cell count decreased			
subjects affected / exposed	2 / 21 (9.52%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 21 (9.52%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Headache			

subjects affected / exposed	2 / 21 (9.52%)	1 / 3 (33.33%)	0 / 11 (0.00%)
occurrences (all)	2	1	0
Sciatica			
subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Anaemia			
subjects affected / exposed	3 / 21 (14.29%)	1 / 3 (33.33%)	0 / 11 (0.00%)
occurrences (all)	3	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 21 (14.29%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Vomiting			
subjects affected / exposed	4 / 21 (19.05%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Abdominal pain upper			
subjects affected / exposed	2 / 21 (9.52%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	1 / 21 (4.76%)	1 / 3 (33.33%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Hair colour changes			
subjects affected / exposed	1 / 21 (4.76%)	2 / 3 (66.67%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Pruritus			
subjects affected / exposed	1 / 21 (4.76%)	2 / 3 (66.67%)	0 / 11 (0.00%)
occurrences (all)	1	2	0
Skin discolouration			
subjects affected / exposed	0 / 21 (0.00%)	1 / 3 (33.33%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Urticaria			

subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Urinary retention			
subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Arthralgia			
subjects affected / exposed	4 / 21 (19.05%)	0 / 3 (0.00%)	2 / 11 (18.18%)
occurrences (all)	4	0	2
Back pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 3 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	2
Intervertebral disc protrusion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Infections and infestations			
Sinusitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 3 (33.33%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			

subjects affected / exposed	4 / 21 (19.05%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
COVID-19			
subjects affected / exposed	7 / 21 (33.33%)	2 / 3 (66.67%)	1 / 11 (9.09%)
occurrences (all)	7	2	1
Tooth infection			
subjects affected / exposed	2 / 21 (9.52%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Cellulitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 3 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 3 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 3 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 February 2022	Updated language regarding schedule of events, protocol synopsis, dose regimen, safety reporting and assessments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported