Clinical trial results:
A Phase 2, Proof-of-Concept, Randomized, Double-Blinded, Placebo-Controlled Study of ACH-0144471 Treatment for 6 Months in Patients with C3 Glomerulopathy (C3G), with an Open-label Extension

Summary

EudraCT number	2017-000663-33
Trial protocol	GB
Global end of trial date	18 December 2020

Results information

Result version number	v1
This version publication date	25 June 2021
First version publication date	25 June 2021

Trial information

Trial identification

Sponsor protocol code	ACH471-204

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03369236
WHO universal trial number (UTN)	U1111-1203-9076

Notes:

Sponsors

Sponsor organisation name	Alexion Pharmaceuticals, Inc
Sponsor organisation address	121 Seaport Boulevard, Boston, MA, United States, 02210
Public contact	European Clinical Trial Information, Alexion Pharmaceuticals, Inc, +33 147100606, clinicaltrials.eu@alexion.com
Scientific contact	European Clinical Trial Information, Alexion Pharmaceuticals, Inc, +33 147100606, clinicaltrials.eu@alexion.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002310-PIP02-17
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	26 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 December 2019
Global end of trial reached?	Yes
Global end of trial date	18 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy, relative to placebo, of 6 months of oral treatment with ACH-0144471 (also known as danicopan and ALXN2040) in participants with C3G based on:
• Renal biopsy results
• Improvement relative to baseline in proteinuria

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of Good Clinical Practice (GCP), according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Harmonized Tripartite Guideline, 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	15 March 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	21 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	13
EEA total number of subjects	0

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)	2
Adults (18-64 years)	11
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

To enroll in the study, participants were required to have a biopsy confirmed diagnosis of C3G, with initial diagnosis made at least 3 months prior to dosing and significant proteinuria.

Period 1

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

Blinding implementation details:

Participants were randomized 1:1 to treatment with danicopan or placebo during the 6-month double-blind treatment period.

Arms

Are arms mutually exclusive?	Yes
Arm title	Danicopan (Double-blind Treatment Period)

Arm description:

Danicopan was administered at a starting dose of 100 mg 3 times daily (TID) for the first 2 weeks, then dosage was to be increased to 200 mg TID for the remainder of the 6-month treatment period.

Arm type	Active comparator
Investigational medicinal product name	Danicopan
Investigational medicinal product code	
Other name	ACH-4471, ACH4471, 4471, ALXN2040
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Danicopan was administered TID.

Arm title	Placebo (Double-blind Treatment Period)

Arm description:

Placebo was administered TID during the 6-month treatment period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo was administered TID.

Number of subjects in period 1	Danicopan (Double-blind Treatment Period)	Placebo (Double-blind Treatment Period)
Started	6	7
Received at least 1 dose of study drug	6	7
Completed	6	6
Not completed	0	1
Accidental unblinding	-	1

Period 2

Period 2 title	Open-label Extension period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Danicopan (Open-label Extension)

Arm description:

All participants who completed the double-blind treatment period were enrolled in the open-label extension period and were to receive danicopan 200 mg TID.

Arm type	Experimental
Investigational medicinal product name	Danicopan
Investigational medicinal product code	
Other name	ACH-4471, ACH4471, 4471, ALXN2040
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Danicopan 200 mg was administered TID.

Number of subjects in period 2	Danicopan (Open-label Extension)
Started	12
Received at least 1 dose of study drug	12
Completed	1
Not completed	11
Sponsor decision to close study	7
Adverse event, non-fatal	1
Lack of efficacy	3

Baseline characteristics

Reporting groups	
Reporting group title	Danicopan (Double-blind Treatment Period)
Reporting group description:	
Danicopan was administered at a starting dose of 100 mg 3 times daily (TID) for the first 2 weeks, then dosage was to be increased to 200 mg TID for the remainder of the 6-month treatment period.	
Reporting group title	Placebo (Double-blind Treatment Period)
Reporting group description:	
Placebo was administered TID during the 6-month treatment period.	

Reporting group values	Danicopan (Double-blind Treatment Period)	Placebo (Double-blind Treatment Period)	Total
Number of subjects	6	7	13
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	1	1	2
Adults (18-64 years)	5	6	11
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	25.5	24.9	
standard deviation	± 10.54	± 4.85	-
Gender categorical Units: Subjects			
Female	2	2	4
Male	4	5	9
Race Units: Subjects			
Asian	0	2	2
White	5	4	9
Other	1	1	2
Ethnicity Units: Subjects			
Hispanic or Latino	3	1	4
Not Hispanic or Latino	3	6	9

End points

End points reporting groups

Reporting group title	Danicopan (Double-blind Treatment Period)

Reporting group description:

Danicopan was administered at a starting dose of 100 mg 3 times daily (TID) for the first 2 weeks, then dosage was to be increased to 200 mg TID for the remainder of the 6-month treatment period.

Reporting group title	Placebo (Double-blind Treatment Period)

Reporting group description:

Placebo was administered TID during the 6-month treatment period.

Reporting group title	Danicopan (Open-label Extension)

Reporting group description:

All participants who completed the double-blind treatment period were enrolled in the open-label extension period and were to receive danicopan 200 mg TID.

Subject analysis set title	Danicopan (Double-blind Treatment), Danicopan (Open-label)
Subject analysis set type	Full analysis

Subject analysis set description:

Danicopan was administered at a starting dose of 100 mg TID for the first 2 weeks, then dosage was to be increased to 200 mg TID for the remainder of the 6-month treatment period.
All participants who completed the double-blind treatment period were enrolled in the open-label extension period and were to receive danicopan 200 mg TID.

Subject analysis set title	Placebo (Double-blind Treatment), Danicopan (Open-label)
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo was administered TID during the 6-month treatment period.
All participants who completed the double-blind treatment period were enrolled in the open-label extension period and were to receive danicopan 200 mg TID.

Primary: Change From Baseline In Composite Biopsy Score At Week 28

End point title	Change From Baseline In Composite Biopsy Score At Week

End point description:

The composite biopsy score was based on a score incorporating changes in the activity index, glomerular C3c staining, and glomerular macrophage infiltration at the end of 6 months of treatment. The composite renal biopsy index scoring system ranged from 0 to 21, with higher scores indicating worse outcomes.

End point type	Primary

End point timeframe:

Baseline, Week 28

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: Mean values and mean change from baseline were summarized descriptively by treatment group.

End point values	Danicopan (Double-blind Treatment Period)	Placebo (Double-blind Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6[2]		
Units: score on a scale				
arithmetic mean (standard deviation)				

Baseline	11.7 (± 4.23)	9.3 (± 3.50)		
Week 28	9.2 (± 4.87)	10.7 (± 3.39)		
Change from Baseline	-2.0 (± 1.87)	1.3 (± 2.88)		

Notes:

[2] - Week 28: n=5

Statistical analyses

No statistical analyses for this end point

Primary: Participants With Reduction In Proteinuria At Week 28

End point title	Participants With Reduction In Proteinuria At Week 28[3]

End point description:

Proteinuria reduction was defined as ≥ 30% decrease from baseline based on 24-hour urine protein (mg/day).

End point type	Primary

End point timeframe:

Week 28

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: Mean values and mean change from baseline were summarized descriptively by treatment group.

End point values	Danicopan (Double-blind Treatment Period)	Placebo (Double-blind Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: participants				
number (not applicable)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In Proteinuria At Week 28

End point title	Change From Baseline In Proteinuria At Week 28

End point description:

Proteinuria was assessed based on 24-hour urine collections at baseline and Week 28.

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Danicopan (Double-blind Treatment Period)	Placebo (Double-blind Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[4]	7[5]		
Units: mg/day				
arithmetic mean (standard deviation)				
Baseline	6137.67 (± 2904.359)	4274.47 (± 2992.819)		
Week 28	5301.75 (± 2984.445)	5186.80 (± 4069.279)		
Change from Baseline	302.00 (± 764.211)	182.20 (± 994.558)		

Notes:

[4] - Week 28: n=4

[5] - Week 28: n=5

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline In Proteinuria At Week 28

End point title	Percent Change From Baseline In Proteinuria At Week 28

End point description:

Proteinuria was assessed based on 24-hour urine collections at baseline and Week 28.

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Danicopan (Double-blind Treatment Period)	Placebo (Double-blind Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	5		
Units: percent change				
arithmetic mean (standard deviation)	12.5 (± 31.11)	-10.4 (± 31.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: Slope Of Estimated Glomerular Filtration Rate (eGFR) From Baseline To 6 Months

End point title	Slope Of Estimated Glomerular Filtration Rate (eGFR) From Baseline To 6 Months

End point description:

Slope of eGFR was estimated using a simple linear regression for each participant, including all data

values from baseline until the end of the 6-month treatment period, with eGFR as the dependent variable and time as the independent variable.

End point type	Secondary

End point timeframe:

6 months

End point values	Danicopan (Double-blind Treatment Period)	Placebo (Double-blind Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: mL/min/1.73 m^2 per month				
arithmetic mean (standard deviation)	-2.26840 (± 1.790814)	-1.45421 (± 2.228395)		

Statistical analyses

No statistical analyses for this end point

Secondary: Slope Of Estimated Glomerular Filtration Rate (eGFR) After Open-label Danicopan

End point title	Slope Of Estimated Glomerular Filtration Rate (eGFR) After Open-label Danicopan

End point description:

Slope of eGFR was estimated using a simple linear regression for each participant, including all data values during the open-label extension period with eGFR as the dependent variable and time as the independent variable.

End point type	Secondary

End point timeframe:

12 months

End point values	Danicopan (Open-label Extension)			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: mL/min/1.73 m^2 per month				
arithmetic mean (standard deviation)	-1.39169 (± 2.401039)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In eGFR At Week 28

End point title	Change From Baseline In eGFR At Week 28

End point description:

Change from baseline in eGFR at Week 28 is presented.

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Danicopan (Double-blind Treatment Period)	Placebo (Double-blind Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7[6]		
Units: mL/min/1.73 m^2				
arithmetic mean (standard deviation)				
Baseline	79.890 (± 44.4571)	68.381 (± 36.7249)		
Week 28	67.543 (± 47.8062)	50.874 (± 15.0517)		
Change from Baseline	-12.347 (± 10.8063)	-8.700 (± 16.0990)		

Notes:

[6] - Week 28: n=5

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With Significant Improvement In eGFR Relative To Baseline At Week 28

End point title	Participants With Significant Improvement In eGFR Relative To Baseline At Week 28

End point description:

Significant improvement relative to baseline was defined as a ≥ 20% increase from baseline in eGFR.

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Danicopan (Double-blind Treatment Period)	Placebo (Double-blind Treatment Period)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	5		
Units: participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants With Significant Improvement In eGFR Relative To Baseline At Week 52

End point title	Participants With Significant Improvement In eGFR Relative To Baseline At Week 52

End point description:

Significant improvement relative to baseline was defined as a ≥ 20% increase from baseline in eGFR.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Danicopan (Double-blind Treatment), Danicopan (Open-label)	Placebo (Double-blind Treatment), Danicopan (Open-label)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	5		
Units: participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 (after dosing) through Week 28 (treatment period and follow-up) and Week 104 (open-label extension and follow-up). The median study duration was 548.0 days.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Danicopan (Double-blind Treatment Period)
Reporting group description:	
Danicopan was administered at a starting dose of 100 mg TID for the first 2 weeks, then dosage was to be increased to 200 mg TID for the remainder of the 6-month treatment period.	
Reporting group title	Placebo (Double-Blind Treatment Period)
Reporting group description:	
Placebo was administered TID during the 6-month treatment period.	
Reporting group title	Danicopan (Open-label Extension Period)
Reporting group description:	
All participants who received danicopan or placebo in the treatment period were to receive danicopan 200 mg TID during the open-label extension period.	

Serious adverse events	Danicopan (Double-blind Treatment Period)	Placebo (Double-Blind Treatment Period)	Danicopan (Open-label Extension Period)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 13 (7.69%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Danicopan (Double-blind Treatment Period)	Placebo (Double-Blind Treatment Period)	Danicopan (Open-label Extension Period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	5 / 7 (71.43%)	8 / 13 (61.54%)

Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Orthostatic hypotension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pallor			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Feeling cold			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Social circumstances			
Pregnancy of partner			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Perineal pain			

subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	2 / 6 (33.33%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	3	0	0
Oropharyngeal pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Cough			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract congestion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Paranasal sinus discomfort			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Nightmare			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	1 / 13 (7.69%)
occurrences (all)	2	1	1
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	0 / 6 (0.00%)	2 / 7 (28.57%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Hand fracture			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Skin laceration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Joint injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Dizziness postural			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Lethargy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Memory impairment			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Eye disorders			

Eye pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	2 / 7 (28.57%)	1 / 13 (7.69%)
occurrences (all)	2	2	1
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	2 / 7 (28.57%)	1 / 13 (7.69%)
occurrences (all)	1	3	1
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	2 / 13 (15.38%)
occurrences (all)	1	0	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Macule			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Joint effusion			

subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Arthropathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	3	1	0
Gastroenteritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 7 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 7 (14.29%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 7 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	3

Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 7 (0.00%) 0	1 / 13 (7.69%) 1
Metabolism and nutrition disorders Gout subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 7 (0.00%) 0	0 / 13 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 October 2017	• Allowed visits on Weeks 14, 18, 22, and 26 to be conducted by phone rather than in the clinic, at the discretion of the investigator, in order to reduce the burden on participants in the study.
12 December 2017	• Allowed investigators who wished to do so to collect measured glomerular filtration rate (GFR) in addition to the existing eGFR calculations. • The contraception requirements were modified to align with updated standard wording, and serious adverse event reporting contact information was updated.
07 March 2018	• Changed improvement in eGFR from a primary to a secondary objective and aligned endpoints with this change. • Adjusted inclusion/exclusion criteria related to complement components in order to facilitate enrollment of suitable participants. • Removed the planned collection pharmacokinetic profile samples on Day 3 in order to reduce the burden on participants. • The contraception requirements were modified to align with updated standard wording. • Vaccination procedures were updated to refer to national and/or local guidelines, minor wording changes are being made for clarity.
15 February 2019	• Made changes to the inclusion and exclusion criteria to better reflect the intended participant population and to facilitate enrollment. • Changed the dose escalation strategy, so that all participants will escalate after 2 weeks. • Reduced sample collection and added flexibility to the collection schedule to reduce the burden on participants (including making collection of renal biopsies an optional sub-study).
05 June 2019	• Made changes to the inclusion and exclusion criteria to remove the allowance of adolescents in the study population. • Reduced sample collection and added flexibility to the collection schedule to reduce the burden on participants. • Removed the biopsy sub-study option (all participants had biopsy-confirmed diagnosis). • Extended the study to Week 104 (addition of a 12-month long- term follow-up period). • Removed Data and Safety Monitoring Board since the study is only blinded to the Investigator, site staff and participants (Sponsor not blinded). • Reduced the number of in-clinic study visits by having the ability to do visits as phone calls. • Reduced the number of expected patients to 20.
15 May 2020	• Increased duration of study treatment. • Allowed home and telephone visits, local laboratory testing, and study drug to be sent directly to participant’s home when clinic visits were not possible due to COVID-19 global pandemic. • Allowed optional renal biopsy at Week 52 and Week 104 to be postponed due to COVID-19 global pandemic, and to be performed when possible. • Updated contraceptive language to align with most recent Investigator Brochure.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None.

Notes: