



## Clinical trial results:

### An Open-Label Phase 2 Proof-of-Concept Study in Patients with C3 Glomerulopathy (C3G) or Immune-Complex Membranoproliferative Glomerulonephritis (IC-MPGN) Treated with ACH-0144471

#### Summary

EudraCT number	2017-002674-39
Trial protocol	BE NL IT
Global end of trial date	29 March 2021

#### Results information

Result version number	v1 (current)
This version publication date	29 September 2021
First version publication date	29 September 2021

#### Trial information

##### Trial identification

Sponsor protocol code	ACH471-205
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03459443
WHO universal trial number (UTN)	U1111-1203-9136

Notes:

#### Sponsors

Sponsor organisation name	Achillion Pharmaceuticals, Inc. (a subsidiary of 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)	EMA-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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	18 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 March 2021
Global end of trial reached?	Yes
Global end of trial date	29 March 2021
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

The primary purpose of this study was to evaluate the efficacy of 12 months of oral ACH 0144471 (also known as danicopan and ALXN2040) in participants with C3G or IC-MPGN based on histologic scoring and 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	14 May 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	27 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	22
EEA total number of subjects	14

Notes:

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**Subjects enrolled per age group**

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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)	5
Adults (18-64 years)	17
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 biopsy-confirmed primary C3G or IC-MPGN and clinical evidence of ongoing disease based on significant proteinuria.

### Period 1

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

### Arms

Arm title	Danicopan
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Arm description:

Danicopan was to be administered to participants with C3G or IC-MPGN at a starting dose of 100 milligrams (mg) 3 times daily (TID) for the first 2 weeks, then the dosage was to be increased to 200 mg TID for the remainder of the study.

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 was administered for up to 40 months, which included an initial 12-month Treatment Period and up to 27-month Long-term Extension.

Number of subjects in period 1	Danicopan
Started	22
Received at Least 1 Dose of Study Drug	22
Completed	0
Not completed	22
Adverse event, non-fatal	1
Lack of efficacy	3
Sponsor's decision to close the study	18

## Baseline characteristics

### Reporting groups

Reporting group title	Danicopan
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Reporting group description:

Danicopan was to be administered to participants with C3G or IC-MPGN at a starting dose of 100 milligrams (mg) 3 times daily (TID) for the first 2 weeks, then the dosage was to be increased to 200 mg TID for the remainder of the study.

Reporting group values	Danicopan	Total	
Number of subjects	22	22	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	5	5	
Adults (18-64 years)	17	17	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	24.3		
standard deviation	± 9.90	-	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	12	12	

## End points

### End points reporting groups

Reporting group title	Danicopan
Reporting group description: Danicopan was to be administered to participants with C3G or IC-MPGN at a starting dose of 100 milligrams (mg) 3 times daily (TID) for the first 2 weeks, then the dosage was to be increased to 200 mg TID for the remainder of the study.	

### Primary: Change From Baseline In Composite Biopsy Score At End Of Initial 12-Month Treatment Period

End point title	Change From Baseline In Composite Biopsy Score At End Of Initial 12-Month Treatment Period <sup>[1]</sup>
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 the initial 12 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, end of initial 12-Month Treatment Period	
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: Endpoint was summarized descriptively.	

End point values	Danicopan			
Subject group type	Reporting group			
Number of subjects analysed	16 <sup>[2]</sup>			
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline	10.6 (± 3.59)			
End of 12-Month Initial Treatment Period	8.0 (± 4.53)			
Change from Baseline	-0.9 (± 1.89)			

Notes:  
[2] - End of 12-Month Initial Treatment Period: n=9

### Statistical analyses

No statistical analyses for this end point

### Primary: Participants With Reduction In Proteinuria At End Of Initial 12-Month Treatment Period

End point title	Participants With Reduction In Proteinuria At End Of Initial 12-Month Treatment Period <sup>[3]</sup>
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:

Baseline, end of initial 12-Month Treatment Period

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: Endpoint was summarized descriptively.

<b>End point values</b>	Danicopan			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: participants				
number (not applicable)	8			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline In Proteinuria At End Of Initial 12-Month Treatment Period

End point title	Change From Baseline In Proteinuria At End Of Initial 12-Month Treatment Period
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End point description:

Proteinuria was assessed based on 24-hour urine collections at baseline and end of the initial 12-Month Treatment Period.

End point type	Secondary
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End point timeframe:

Baseline, end of initial 12-Month Treatment Period

<b>End point values</b>	Danicopan			
Subject group type	Reporting group			
Number of subjects analysed	22 <sup>[4]</sup>			
Units: mg/day				
arithmetic mean (standard deviation)				
Baseline	4252.28 (± 2684.959)			
End of Initial 12-Month Treatment Period	3512.63 (± 3335.765)			
Change from Baseline	-671.11 (± 2695.592)			

Notes:

[4] - End of the initial 12-Month Treatment Period: 19

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Change From Baseline In Proteinuria At End Of Initial 12-Month

## Treatment Period

End point title	Percent Change From Baseline In Proteinuria At End Of Initial 12-Month Treatment Period
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End point description:

Proteinuria was assessed based on 24-hour urine collections at baseline and end of initial 12-Month Treatment Period.

End point type	Secondary
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End point timeframe:

Baseline, end of initial 12-Month Treatment Period

<b>End point values</b>	Danicopan			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: percent change				
arithmetic mean (standard deviation)	-17.1 (± 53.17)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Slope Of Estimated Glomerular Filtration Rate (eGFR) From Baseline To End Of Initial 12-Month Treatment Period

End point title	Slope Of Estimated Glomerular Filtration Rate (eGFR) From Baseline To End Of Initial 12-Month Treatment Period
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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 Initial 12-Month Treatment Period, with eGFR as the dependent variable and time as the independent variable.

End point type	Secondary
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End point timeframe:

End of initial 12-Month Treatment Period

<b>End point values</b>	Danicopan			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: mL/min/1.73 m <sup>2</sup> per month				
arithmetic mean (standard deviation)	-1.24917 (± 1.811457)			

## Statistical analyses



No statistical analyses for this end point

### Secondary: Change From Baseline In eGFR At End Of Initial 12-Month Treatment Period

End point title	Change From Baseline In eGFR At End Of Initial 12-Month Treatment Period
End point description: Change from baseline in eGFR at end of initial 12-Month Treatment Period is presented.	
End point type	Secondary
End point timeframe: Baseline, end of initial 12-Month Treatment Period	

End point values	Danicopan			
Subject group type	Reporting group			
Number of subjects analysed	22 <sup>[5]</sup>			
Units: mL/min/1.73 m <sup>2</sup>				
arithmetic mean (standard deviation)				
Baseline	90.692 (± 35.4939)			
End of Initial 12-Month Treatment Period	81.412 (± 38.3320)			
Change from Baseline	-9.795 (± 14.3806)			

Notes:

[5] - End of the initial 12-month Treatment Period: n=20

### Statistical analyses

No statistical analyses for this end point

### Secondary: Participants With Significant Improvement In eGFR Relative To Baseline At End Of Initial 12-Month Treatment Period

End point title	Participants With Significant Improvement In eGFR Relative To Baseline At End Of Initial 12-Month Treatment Period
End point description: Significant improvement relative to baseline was defined as a ≥ 25% increase from baseline in eGFR.	
End point type	Secondary
End point timeframe: Baseline, End Of Initial 12-Month Treatment Period	

End point values	Danicopan			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: participants				
number (not applicable)	0			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline In eGFR Over 12 Months Of Treatment For Participants Meeting eGFR Inclusion Criteria At Study Entry

End point title	Change From Baseline In eGFR Over 12 Months Of Treatment For Participants Meeting eGFR Inclusion Criteria At Study Entry
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End point description:

End point type	Secondary
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End point timeframe:

End of initial 12-Month Treatment Period

<b>End point values</b>	Danicopan			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[6]</sup>			
Units: mL/min/1.73 m <sup>2</sup>				
arithmetic mean (standard deviation)	( )			

Notes:

[6] - No participants met the criteria.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline In Measured GFR At The End Of The Initial 12-Month Treatment Period

End point title	Change From Baseline In Measured GFR At The End Of The Initial 12-Month Treatment Period
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End point description:

End point type	Secondary
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End point timeframe:

End of initial 12-Month Treatment Period

<b>End point values</b>	Danicopan			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[7]</sup>			
Units: mL/min/1.73 m <sup>2</sup>				
arithmetic mean (standard deviation)				
Baseline	()			
End of initial 12-Month Treatment Period	()			
Change from Baseline	()			

Notes:

[7] - No participants met criteria.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 1 (after dosing) through up to 40 months. The mean study duration was 569.0 days.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.0
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### Reporting groups

Reporting group title	Danicopan
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Reporting group description:

Danicopan was to be administered to participants with C3G or IC-MPGN at a starting dose of 100 mg TID for the first 2 weeks, then the dosage was to be increased to 200 mg TID for the remainder of the study.

Serious adverse events	Danicopan		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 22 (13.64%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Rhinovirus infection			

subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Danicopan		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 22 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Hypertensive crisis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	3		
Arteriovenous fistula			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Haematoma			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Hot flush			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Pallor			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Surgical and medical procedures			

Sinus operation subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Pregnancy, puerperium and perinatal conditions Pregnancy subjects affected / exposed <sup>[1]</sup> occurrences (all)	1 / 10 (10.00%) 1		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)  Oedema peripheral subjects affected / exposed occurrences (all)  Fatigue subjects affected / exposed occurrences (all)  Asthenia subjects affected / exposed occurrences (all)  Influenza like illness subjects affected / exposed occurrences (all)  Chills subjects affected / exposed occurrences (all)  Facial pain subjects affected / exposed occurrences (all)  Localised oedema subjects affected / exposed occurrences (all)  Non-cardiac chest pain subjects affected / exposed occurrences (all)  Oedema	11 / 22 (50.00%) 16  8 / 22 (36.36%) 15  5 / 22 (22.73%) 7  4 / 22 (18.18%) 5  1 / 22 (4.55%) 2  1 / 22 (4.55%) 1  1 / 22 (4.55%) 1  1 / 22 (4.55%) 1  1 / 22 (4.55%) 1		

subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Pain subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Multiple allergies subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Reproductive system and breast disorders Menstruation irregular subjects affected / exposed <sup>[2]</sup> occurrences (all)	2 / 10 (20.00%) 2		
Oligomenorrhoea subjects affected / exposed <sup>[3]</sup> occurrences (all)	1 / 10 (10.00%) 1		
Premature menopause subjects affected / exposed <sup>[4]</sup> occurrences (all)	1 / 10 (10.00%) 1		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	5 / 22 (22.73%) 8		
Dyspnoea subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 5		
Cough subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 4		
Rhinorrhoea subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3		
Productive cough			

subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Nasal congestion			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Dysphonia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Upper-airway cough syndrome			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Wheezing			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Abnormal dreams			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Blood potassium decreased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Blood uric acid increased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Crystal urine present			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Electrocardiogram QT prolonged			



subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Haemoglobin decreased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Lipids increased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Transaminases increased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Blood creatine phosphokinase increased			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	11		
Blood creatinine increased			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Blood potassium increased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Lip injury			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Post procedural haematuria			

subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Cardiac disorders			
Palpitations			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Left ventricular failure			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 22 (27.27%)		
occurrences (all)	13		
Dizziness			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Migraine			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Syncope			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Restless legs syndrome			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Dizziness postural			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Migraine with aura			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Taste disorder			

subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	5		
Leukopenia			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Thrombocytosis			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Anaemia macrocytic			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Leukocytosis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Neutrophilia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Vertigo			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Eye disorders			
Periorbital oedema			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Conjunctivitis allergic			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Vision blurred			

subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	6 / 22 (27.27%)		
occurrences (all)	7		
Diarrhoea			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	7		
Nausea			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Abdominal distension			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Abdominal pain lower			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Bowel movement irregularity			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		

Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Haemorrhoids			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Hypertrophy of tongue papillae			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Paraesthesia oral			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Retroperitoneal haematoma			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Pruritus			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Erythema			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Acne			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Alopecia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Dermatitis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Dermatitis atopic			

subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Ingrowing nail subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Rash erythematous subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Skin lesion subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Renal and urinary disorders Renal impairment subjects affected / exposed occurrences (all)	5 / 22 (22.73%) 6		
Acute kidney injury subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Nephrotic syndrome subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Endocrine disorders Hyperparathyroidism secondary subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Hypothyroidism subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 5		
Back pain subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3		
Pain in extremity			

subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Musculoskeletal chest pain			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Myalgia			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Arthralgia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Bone pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Joint effusion			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Muscle tightness			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Pain in jaw			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Rhabdomyolysis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	6 / 22 (27.27%)		
occurrences (all)	11		

Pharyngitis			
subjects affected / exposed	6 / 22 (27.27%)		
occurrences (all)	6		
Influenza			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Nasopharyngitis			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	9		
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	4		
Urinary tract infection			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	4		
Bronchitis			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Rhinitis			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Tonsillitis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Viral infection			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Bacteriuria			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		



Corona virus infection subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Ear lobe infection subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Enterobiasis subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Herpes zoster subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Impetigo subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Respiratory tract infection viral subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Sinusitis subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Metabolism and nutrition disorders			
Hyperkalaemia subjects affected / exposed occurrences (all)	5 / 22 (22.73%) 10		
Hyperphosphataemia subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Metabolic acidosis subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Vitamin D deficiency subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Decreased appetite			

subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Dehydration			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Dyslipidaemia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Hyperuricaemia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Hypovitaminosis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Iron deficiency			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Adverse event occurs in only female participants.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Adverse event occurs in only female participants.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Adverse event occurs in only female participants.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Adverse event occurs in only female participants.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2017	<ul style="list-style-type: none"><li>Allowed Investigators who wished to do so to collect measured glomerular filtration rate (GFR) in addition to the existing eGFR calculations.</li><li>Modified contraception requirements, and serious adverse event (SAEs) reporting contact information was updated.</li></ul>
23 March 2018	<ul style="list-style-type: none"><li>Allowed vaccinations to be administered according to local/national guidelines.</li><li>Removed intensive pharmacokinetic (PK) sampling at Day 3 in order to reduce the burden to study participants; trough PK sample on Day 3 was retained.</li><li>Simplified the complement based inclusion/exclusion criteria.</li><li>Updated contact information for reporting SAEs.</li></ul>
30 January 2019	<ul style="list-style-type: none"><li>Revised the primary objective to include only improvement in proteinuria and changed improvement in eGFR to a secondary objective.</li><li>Made changes to the inclusion and exclusion criteria to better reflect the intended patient population and to facilitate enrollment.</li><li>Changed the dose escalation strategy so that all participants would escalate after 2 weeks.</li><li>Reduced sample collection and added flexibility to the collection schedule to reduce the burden on participants.</li></ul>
22 July 2019	<ul style="list-style-type: none"><li>Added biopsy as a primary endpoint.</li><li>Reduced sample collection and added flexibility to the collection schedule to reduce the burden on participants.</li><li>Removed the biopsy sub study option at Week 52.</li><li>Extended the study to Week 104 (addition of a 12-month Long term Follow up Period).</li><li>Reduced the number of in clinic study visits by allowing visits by phone call.</li></ul>
15 May 2020	<ul style="list-style-type: none"><li>Increased duration of study treatment from 24 to 40 months.</li><li>Updated stopping rules for individual participants.</li><li>Allowed home and telephone visits, local laboratory testing, and study intervention to be sent directly to participants' homes when clinic visits were not possible due to the coronavirus disease 2019 (COVID 19) global pandemic.</li><li>Allowed optional renal biopsy to be performed when possible due to COVID 19 global pandemic.</li><li>Updated contraceptive language to align with the most recent Investigator Brochure.</li></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported