



## Clinical trial results:

### A Phase 2 Open-label Study of ACH-0144471 in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) Who Have an Inadequate Response to Eculizumab Monotherapy

#### Summary

EudraCT number	2016-003526-16
Trial protocol	GB IT
Global end of trial date	05 January 2023

#### Results information

Result version number	v1 (current)
This version publication date	14 December 2023
First version publication date	14 December 2023

#### Trial information

##### Trial identification

Sponsor protocol code	ACH471-101
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03472885
WHO universal trial number (UTN)	U1111-1209-4655

Notes:

##### Sponsors

Sponsor organisation name	Alexion Pharmaceuticals, Inc.
Sponsor organisation address	121 Seaport Blvd, Boston, MA, United States, 02210
Public contact	Alexion Europe SAS European Clinical Trial Information, Alexion Pharmaceuticals Inc., +33 787148158, clinicaltrials.eu@alexion.com
Scientific contact	Alexion Europe SAS European Clinical Trial Information, Alexion Pharmaceuticals Inc., +33 787148158, clinicaltrials.eu@alexion.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	05 January 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	05 January 2023
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To determine the effectiveness of ACH-0144471 (also known as danicopan and ALXN2040) in improving anemia, as measured by increased blood hemoglobin, when given with eculizumab (a drug commonly used for treatment of PNH) for 24 weeks in participants with PNH.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, 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	08 May 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	United Kingdom: 4
Worldwide total number of subjects	12
EEA total number of subjects	2

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)	10
From 65 to 84 years	2
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study included a 24-Week Treatment Period and Long-term Extension (LTE) Period.

### Period 1

Period 1 title	24-Week Treatment Period
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

### Arms

<b>Arm title</b>	Danicopan + Eculizumab
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Arm description:

Participants were administered 100, 150, or 200 milligrams (mg) danicopan three times daily (TID) in combination with eculizumab for 24 weeks. Danicopan dose may have been increased within each participant, to a maximum of 200 mg TID based on safety and efficacy. After completing the 24-Week Treatment Period, participants who received clinical benefit (as assessed by the Investigator based on improvement in hemoglobin) continued into the LTE and received the same dose of danicopan plus eculizumab treatment as that received at the end of the 24-Week Treatment Period.

Arm type	Experimental
Investigational medicinal product name	Eculizumab
Investigational medicinal product code	
Other name	Soliris
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eculizumab was administered per schedule specified in the arm description.

Investigational medicinal product name	Danicopan
Investigational medicinal product code	ACH-0144471
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Danicopan was administered per schedule specified in the arm description.

Number of subjects in period 1	Danicopan + Eculizumab
Started	12
Safety Population	12
Efficacy Population	11
Completed	11
Not completed	1
Adverse event, non-fatal	1

<b>Period 2</b>	
Period 2 title	LTE Period (Maximum Exposure: 1463 Days)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

## Arms

<b>Arm title</b>	Danicopan + Eculizumab
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Arm description:

Participants were administered 100, 150, or 200 milligrams (mg) danicopan three times daily (TID) in combination with eculizumab for 24 weeks. Danicopan dose may have been increased within each participant, to a maximum of 200 mg TID based on safety and efficacy. After completing the 24-Week Treatment Period, participants who received clinical benefit (as assessed by the Investigator based on improvement in hemoglobin) continued into the LTE and received the same dose of danicopan plus eculizumab treatment as that received at the end of the 24-Week Treatment Period.

Arm type	Experimental
Investigational medicinal product name	Eculizumab
Investigational medicinal product code	
Other name	Soliris
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eculizumab was administered per schedule specified in the arm description.

Investigational medicinal product name	Danicopan
Investigational medicinal product code	ACH-0144471
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Danicopan was administered per schedule specified in the arm description.

<b>Number of subjects in period 2</b>	Danicopan + Eculizumab
Started	11
Completed	11

## Baseline characteristics

### Reporting groups

Reporting group title	Danicopan + Eculizumab
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Reporting group description:

Participants were administered 100, 150, or 200 milligrams (mg) danicopan three times daily (TID) in combination with eculizumab for 24 weeks. Danicopan dose may have been increased within each participant, to a maximum of 200 mg TID based on safety and efficacy. After completing the 24-Week Treatment Period, participants who received clinical benefit (as assessed by the Investigator based on improvement in hemoglobin) continued into the LTE and received the same dose of danicopan plus eculizumab treatment as that received at the end of the 24-Week Treatment Period.

Reporting group values	Danicopan + Eculizumab	Total	
Number of subjects	12	12	
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)	0	0	
Adults (18-64 years)	10	10	
From 65-84 years	2	2	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	45.59		
standard deviation	± 16.385	-	
Sex: Female, Male			
Units: participants			
Female	10	10	
Male	2	2	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	12	12	
Unknown or Not Reported	0	0	
Race/Ethnicity, Customized			
Units: Subjects			
White	7	7	
Asian	1	1	
Black or African American	3	3	
Other	1	1	

## End points

### End points reporting groups

Reporting group title	Danicopan + Eculizumab
Reporting group description: Participants were administered 100, 150, or 200 milligrams (mg) danicopan three times daily (TID) in combination with eculizumab for 24 weeks. Danicopan dose may have been increased within each participant, to a maximum of 200 mg TID based on safety and efficacy. After completing the 24-Week Treatment Period, participants who received clinical benefit (as assessed by the Investigator based on improvement in hemoglobin) continued into the LTE and received the same dose of danicopan plus eculizumab treatment as that received at the end of the 24-Week Treatment Period.	
Reporting group title	Danicopan + Eculizumab
Reporting group description: Participants were administered 100, 150, or 200 milligrams (mg) danicopan three times daily (TID) in combination with eculizumab for 24 weeks. Danicopan dose may have been increased within each participant, to a maximum of 200 mg TID based on safety and efficacy. After completing the 24-Week Treatment Period, participants who received clinical benefit (as assessed by the Investigator based on improvement in hemoglobin) continued into the LTE and received the same dose of danicopan plus eculizumab treatment as that received at the end of the 24-Week Treatment Period.	
Subject analysis set title	24-Week Treatment Period: Danicopan + Eculizumab
Subject analysis set type	Safety analysis
Subject analysis set description: Participants were administered 100, 150, or 200 mg danicopan TID in combination with eculizumab for 24 weeks. Danicopan dose may have been increased within each participant, to a maximum of 200 mg TID based on safety and efficacy.	
Subject analysis set title	LTE Period: Danicopan + Eculizumab
Subject analysis set type	Safety analysis
Subject analysis set description: After completing the 24-Week Treatment Period, participants who received clinical benefit (as assessed by the Investigator based on improvement in hemoglobin) continued into the LTE and received the same dose of danicopan plus eculizumab treatment as that received at the end of the 24-Week Treatment Period.	

### Primary: Change from Baseline In Hemoglobin At Week 24

End point title	Change from Baseline In Hemoglobin At Week 24 <sup>[1]</sup>
End point description: Efficacy Population: All treated participants who received at least 4 weeks of danicopan.	
End point type	Primary
End point timeframe: Baseline, Week 24	

#### 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: Statistical analysis was not planned for this endpoint.

End point values	Danicopan + Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: g/dL				
arithmetic mean (standard deviation)				
Baseline	7.94 (± 1.425)			
Week 24	10.33 (± 1.661)			
Change from Baseline	2.39 (± 1.333)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline In Lactate Dehydrogenase At Week 24

End point title	Change From Baseline In Lactate Dehydrogenase At Week 24
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End point description:

Efficacy Population: All treated participants who received at least 4 weeks of danicopan.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

End point values	Danicopan + Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: IU/L				
arithmetic mean (standard deviation)				
Baseline	244.5 (± 74.40)			
Week 24	239.5 (± 48.48)			
Change from Baseline	-5.0 (± 48.60)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number Of Participants Without RBC Transfusions During 24 Weeks Of Treatment

End point title	Number Of Participants Without RBC Transfusions During 24 Weeks Of Treatment
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End point description:

Efficacy Population: All treated participants who received at least 4 weeks of danicopan.

End point type	Secondary
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End point timeframe:

Within 24 weeks prior to first dose and during 24-week treatment period



<b>End point values</b>	Danicopan + Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: participants				
Within 24 Weeks Prior to First Dose	1			
During 24-Week Treatment Period	10			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number Of Units Of Red Blood Cells (RBCs) Transfused During 24 Weeks Of Treatment

End point title	Number Of Units Of Red Blood Cells (RBCs) Transfused During 24 Weeks Of Treatment
End point description:	
Efficacy Population: All treated participants who received at least 4 weeks of danicopan.	
End point type	Secondary
End point timeframe:	
Within 24 weeks prior to first dose and during 24-week treatment period	

<b>End point values</b>	Danicopan + Eculizumab			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: RBC units				
arithmetic mean (standard deviation)				
Within 24 Weeks Prior to First Dose	4.5 (± 3.96)			
During 24-Week Treatment Period	0.2 (± 0.60)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number Of Participants With Serious Adverse Events (SAEs), Grade 3 And Grade 4 Adverse Events (AEs), And Events Leading To Discontinuation Of Study Drug

End point title	Number Of Participants With Serious Adverse Events (SAEs), Grade 3 And Grade 4 Adverse Events (AEs), And Events Leading To Discontinuation Of Study Drug			
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End point description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. An SAE was an AE that met at least 1 of the following criteria: resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization for AE, persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions, congenital anomaly/birth defect, important medical event or reaction.

The intensity of an AE was graded according to the Common Terminology Criteria for Adverse Events (CTCAE) Adverse Event Severity Grading Table. A summary of SAEs and other non-serious AEs regardless of causality is located in the Reported Adverse Events module. Participants who received at least 1 dose of danicopan were included in the safety assessment.

End point type	Secondary
End point timeframe:	
Day 1 (after dosing) through end of study (maximum exposure: 1631 days)	

End point values	24-Week Treatment Period: Danicopan + Eculizumab	LTE Period: Danicopan + Eculizumab		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	11		
Units: participants				
SAEs	2	7		
Grade 3 AEs	4	6		
Grade 4 AEs	1	1		
AEs Leading to Discontinuation of Study Drug	1	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 end of study (maximum exposure: 1631 days)

Adverse event reporting additional description:

Participants who received at least 1 dose of danicopan were included in the safety assessment.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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### Reporting groups

Reporting group title	LTE Period: Danicopan + Eculizumab
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Reporting group description:

After completing the 24-Week Treatment Period, participants who received clinical benefit (as assessed by the Investigator based on improvement in hemoglobin) continued into the LTE and received the same dose of danicopan plus eculizumab treatment as that received at the end of the 24-Week Treatment Period.

Reporting group title	24-Week Treatment Period: Danicopan + Eculizumab
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Reporting group description:

Participants were administered 100, 150, or 200 mg danicopan TID in combination with eculizumab for 24 weeks. Danicopan dose may have been increased within each participant, to a maximum of 200 mg TID based on safety and efficacy.

Serious adverse events	LTE Period: Danicopan + Eculizumab	24-Week Treatment Period: Danicopan + Eculizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 11 (63.64%)	2 / 12 (16.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Schwannoma			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolysis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haemoglobinuria			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			

subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis viral			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	LTE Period: Danicopan + Eculizumab	24-Week Treatment Period: Danicopan + Eculizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	10 / 12 (83.33%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Thirst			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Feeling abnormal			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Fatigue			

subjects affected / exposed	3 / 11 (27.27%)	2 / 12 (16.67%)	
occurrences (all)	4	2	
Pyrexia			
subjects affected / exposed	4 / 11 (36.36%)	1 / 12 (8.33%)	
occurrences (all)	5	1	
Vaccination site pain			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Pain			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	3	0	
Chest discomfort			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Chills			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Influenza like illness			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Immune system disorders			
Seasonal allergy			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Immunisation reaction			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Menorrhagia			

subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders			
Dysphonia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1	
Nasal congestion subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 12 (8.33%) 1	
Oropharyngeal pain alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2	1 / 12 (8.33%) 1	
Cough alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2	0 / 12 (0.00%) 0	
Dyspnoea subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	2 / 12 (16.67%) 2	
Depression subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 12 (8.33%) 1	
Insomnia subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2	1 / 12 (8.33%) 1	
Investigations			
Blood bilirubin increased subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2	1 / 12 (8.33%) 2	
Alanine aminotransferase increased			

subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Fibrin D dimer increased			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Contusion			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Vaccination complication			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Transfusion-associated dyspnoea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Transfusion reaction			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Febrile nonhaemolytic transfusion reaction			



subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Accidental overdose subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Cardiac disorders			
Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1	
Palpitations subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1	
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	5 / 11 (45.45%) 9	3 / 12 (25.00%) 8	
Dizziness subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1	
Anosmia subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2	0 / 12 (0.00%) 0	
Ageusia subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Lethargy subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Memory impairment subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Restless legs syndrome subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Sciatica			

subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Taste disorder subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Disturbance in attention subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 12 (8.33%) 1	
Blood and lymphatic system disorders Anaemia alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1	
Neutropenia subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	2 / 12 (16.67%) 3	
Thrombocytopenia subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 4	0 / 12 (0.00%) 0	
Haemolysis subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Eustachian tube dysfunction subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Tinnitus subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Vertigo subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Eye disorders			

Periorbital swelling subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1	
Gastrointestinal disorders			
Tongue ulceration subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 12 (8.33%) 1	
Nausea subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	2 / 12 (16.67%) 2	
Lip swelling subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1	
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1	
Diarrhoea subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 12 (8.33%) 1	
Abdominal pain subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 2	2 / 12 (16.67%) 3	
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	2 / 12 (16.67%) 2	
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 12 (8.33%) 2	
Dysphagia subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Gingival discomfort subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Mouth ulceration			

subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Oral pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Periodontal disease			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Saliva altered			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	2	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Dermal cyst			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Alopecia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			

Haemoglobinuria subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 4	2 / 12 (16.67%) 2	
Neck pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 12 (8.33%) 2	
Musculoskeletal pain subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	2 / 12 (16.67%) 2	
Arthralgia alternative dictionary used: MedDRA 18.1 subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 3	2 / 12 (16.67%) 2	
Limb discomfort subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 3	0 / 12 (0.00%) 0	
Back pain subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Flank pain subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	1 / 12 (8.33%) 1	
Muscle spasms subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Myalgia subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2	1 / 12 (8.33%) 1	
Infections and infestations			
COVID-19 subjects affected / exposed occurrences (all)	6 / 11 (54.55%) 6	0 / 12 (0.00%) 0	

Upper respiratory tract infection subjects affected / exposed occurrences (all)	5 / 11 (45.45%) 7	5 / 12 (41.67%) 5	
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2	0 / 12 (0.00%) 0	
Conjunctivitis subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2	0 / 12 (0.00%) 0	
Sinusitis subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2	0 / 12 (0.00%) 0	
Cellulitis subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Hordeolum subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Oral herpes subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Pharyngitis subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Metabolism and nutrition disorders Metabolic acidosis subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Hypocalcaemia			

subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2017	This amendment: - Updated the contraception section to include definitions requested by Health Authorities. - Updated the contact information for SAE reporting.
17 January 2018	This amendment provided wording permitting the conducting of patient reported outcomes interviews as questionnaires where required.
13 March 2018	This amendment: - Specified that vaccination against bacterial infections should be performed, when necessary based on vaccination history, according to national and/or local guidelines. - Updated and clarified requirements for "acceptable" and "highly effective" methods of contraception. - Reduced the time window for definition of a missed dose from 6 hours to 4 hours.
15 February 2019	- Amended the exclusion criteria to allow enrollment of participants with a history of hematopoietic stem cell transplant (HSCT) if HSCT engraftment has failed. - Amended the exclusion criteria to allow enrollment of participants with direct bilirubin $> 1.5 \times$ upper limit of normal if the elevated bilirubin is due to extravascular hemolysis, in the opinion of the investigator. - Permitted participants to switch from eculizumab to an approved eculizumab biosimilar or ravulizumab after completion of the primary endpoint at Week 24. - Expanded potential enrolment to a maximum of 14 participants.
19 February 2019	- Shortened the time (from 12 to 8 weeks) for participants to receive a stable dose of eculizumab prior to study entry.
04 June 2021	This amendment: - Updated the dose taper instructions and schedule to remove the 75 mg dose since the 75 mg tablets used in this study would expire and no longer be manufactured. - Added an option for participants to enter another appropriate Alexion clinical study, if available. - Added guidance on dose tapering for participants who enter other clinical studies. - Removed PK and PD samples at the Long term Extension Period clinic visits, Taper Visits, and Follow up Visits. - Added guidance for collection of a predose PK sample for participants who had dose escalation after Week 12. - Updated the language for use of prophylactic antibiotics to recommend use as per local requirements, if applicable. - Added language regarding COVID 19 risk assessment and COVID 19 vaccination risk assessment as per MHRA requirements.

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported