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

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	Efficacy, Safety
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

Arm title	Danicopan + Eculizumab

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

Period 2

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

Arm title	Danicopan + Eculizumab

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 2	Danicopan + Eculizumab
Started	11
Completed	11

Baseline characteristics

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 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[1]

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

End point description:

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

End point type	Secondary

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

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

End point values	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

End point values	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

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	LTE Period: Danicopan + Eculizumab

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

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 %

Non-serious adverse events	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	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Oropharyngeal pain			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 11 (18.18%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Cough			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Dyspnoea			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Depression			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Insomnia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	2	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	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Accidental overdose			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 11 (45.45%)	3 / 12 (25.00%)	
occurrences (all)	9	8	
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Anosmia			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Ageusia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Lethargy			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Memory impairment			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Restless legs syndrome			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Sciatica			

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

Periorbital swelling			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Tongue ulceration			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Lip swelling			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	
occurrences (all)	2	3	
Abdominal discomfort			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Abdominal pain upper			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	2	
Dysphagia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Gingival discomfort			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	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	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 11 (18.18%)	2 / 12 (16.67%)	
occurrences (all)	4	2	
Neck pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Musculoskeletal pain			
subjects affected / exposed	1 / 11 (9.09%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Arthralgia			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	2 / 11 (18.18%)	2 / 12 (16.67%)	
occurrences (all)	3	2	
Limb discomfort			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	3	0	
Back pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Flank pain			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Muscle spasms			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	2 / 11 (18.18%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Infections and infestations			
COVID-19			
subjects affected / exposed	6 / 11 (54.55%)	0 / 12 (0.00%)	
occurrences (all)	6	0	

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

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