



Clinical trial results:

A Phase 2 Open-Label Proof of Concept Study to Assess the Efficacy, Safety, and Pharmacokinetics of the Oral Factor D (FD) Inhibitor ALXN2050 (ACH-0145228) in Paroxysmal Nocturnal Hemoglobinuria (PNH) Patients as Monotherapy

Summary

EudraCT number	2019-003830-17
Trial protocol	GB IT ES
Global end of trial date	20 March 2024

Results information

Result version number	v1 (current)
This version publication date	21 November 2024
First version publication date	21 November 2024

Trial information

Trial identification

Sponsor protocol code	ACH228-110
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04170023
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	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	20 March 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 March 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the efficacy of ALXN2050 based on improvement in hemoglobin (Hgb).

Protection of trial subjects:

This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki, Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines, applicable International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and other applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 December 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	New Zealand: 9
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Türkiye: 3
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Spain: 1
Worldwide total number of subjects	29
EEA total number of subjects	5

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	27
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included a 12-week Treatment Period and a 148-week or 200-week (for sites in New Zealand) Long-term Extension (LTE) Period.

Period 1

Period 1 title	Treatment Period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: Treatment Naive

Arm description:

Participants who were treatment-naive received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.

Arm type	Experimental
Investigational medicinal product name	ALXN2050
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Capsule
Routes of administration	Oral use

Dosage and administration details:

ALXN2050 was administered per schedule specified in the arm description.

Arm title	Group 2: Eculizumab Switch
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Arm description:

Participants who had received component 5 (C5) inhibition with eculizumab for at least 6 months, who continued to experience anemia (Hgb <10 grams/deciliter [dL]) and reticulocytes above the upper limit of normal (ULN), switched to ALXN2050 in this study and received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.

Arm type	Experimental
Investigational medicinal product name	ALXN2050
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

ALXN2050 was administered per schedule specified in the arm description.

Arm title	Group 3: Danicopan Rollover
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Arm description:

Participants who had received danicopan monotherapy during Study ACH471-103 (NCT03181633), switched to ALXN2050 in this study and received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.

Arm type	Experimental
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Investigational medicinal product name	ALXN2050
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

ALXN2050 was administered per schedule specified in the arm description.

Number of subjects in period 1	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover
Started	12	11	6
Received at least 1 dose of study drug	12	11	6
Completed	12	11	6

Period 2

Period 2 title	LTE Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: Treatment Naive

Arm description:

Participants who were treatment-naive received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.

Arm type	Experimental
Investigational medicinal product name	ALXN2050
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

ALXN2050 was administered per schedule specified in the arm description.

Arm title	Group 2: Eculizumab Switch
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Arm description:

Participants who had received component 5 (C5) inhibition with eculizumab for at least 6 months, who continued to experience anemia (hemoglobin [Hgb] <10 grams/deciliter [dL]) and reticulocytes above the upper limit of normal (ULN), switched to ALXN2050 in this study and received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.

Arm type	Experimental
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Investigational medicinal product name	ALXN2050
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use
Dosage and administration details:	
ALXN2050 was administered per schedule specified in the arm description.	
Arm title	Group 3: Danicopan Rollover

Arm description:

Participants who had received danicopan monotherapy during Study ACH471-103 (NCT03181633), switched to ALXN2050 in this study and received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.

Arm type	Experimental
Investigational medicinal product name	ALXN2050
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

ALXN2050 was administered per schedule specified in the arm description.

Number of subjects in period 2	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover
Started	12	11	6
Received at least 1 dose of study drug	12	11	6
Completed	0	0	1
Not completed	12	11	5
Consent withdrawn by subject	1	-	-
Study Termination	11	11	5

Baseline characteristics

Reporting groups

Reporting group title	Group 1: Treatment Naive
Reporting group description:	
Participants who were treatment-naïve received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.	
Reporting group title	Group 2: Eculizumab Switch
Reporting group description:	
Participants who had received component 5 (C5) inhibition with eculizumab for at least 6 months, who continued to experience anemia (Hgb <10 grams/deciliter [dL]) and reticulocytes above the upper limit of normal (ULN), switched to ALXN2050 in this study and received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.	
Reporting group title	Group 3: Danicopan Rollover
Reporting group description:	
Participants who had received danicopan monotherapy during Study ACH471-103 (NCT03181633), switched to ALXN2050 in this study and received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.	

Reporting group values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover
Number of subjects	12	11	6
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean	43.75	42.45	40.50
standard deviation	± 17.099	± 13.419	± 16.718
Sex: Female, Male			
Units: participants			
Female	4	7	3
Male	8	4	3
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	8	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	3	10	6
More than one race	0	0	0
Unknown or Not Reported	1	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	12	10	6
Unknown or Not Reported	0	1	0

HgB Units: grams/liter arithmetic mean standard deviation	81.17 ± 11.731	91.00 ± 9.602	130.67 ± 19.180
Reporting group values	Total		
Number of subjects	29		
Age categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	-		
Sex: Female, Male Units: participants			
Female	14		
Male	15		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	9		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	19		
More than one race	0		
Unknown or Not Reported	1		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	28		
Unknown or Not Reported	1		
HgB Units: grams/liter arithmetic mean standard deviation	-		

End points

End points reporting groups

Reporting group title	Group 1: Treatment Naive
Reporting group description: Participants who were treatment-naive received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.	
Reporting group title	Group 2: Eculizumab Switch
Reporting group description: Participants who had received component 5 (C5) inhibition with eculizumab for at least 6 months, who continued to experience anemia (Hgb <10 grams/deciliter [dL]) and reticulocytes above the upper limit of normal (ULN), switched to ALXN2050 in this study and received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.	
Reporting group title	Group 3: Danicopan Rollover
Reporting group description: Participants who had received danicopan monotherapy during Study ACH471-103 (NCT03181633), switched to ALXN2050 in this study and received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.	
Reporting group title	Group 1: Treatment Naive
Reporting group description: Participants who were treatment-naive received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.	
Reporting group title	Group 2: Eculizumab Switch
Reporting group description: Participants who had received component 5 (C5) inhibition with eculizumab for at least 6 months, who continued to experience anemia (hemoglobin [Hgb] <10 grams/deciliter [dL]) and reticulocytes above the upper limit of normal (ULN), switched to ALXN2050 in this study and received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.	
Reporting group title	Group 3: Danicopan Rollover
Reporting group description: Participants who had received danicopan monotherapy during Study ACH471-103 (NCT03181633), switched to ALXN2050 in this study and received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.	

Primary: Change From Baseline in Hgb at Week 12

End point title	Change From Baseline in Hgb at Week 12 ^[1]
End point description: Hgb baseline was defined as the lowest Hgb value observed between and including screening and first dose date. To address the impact of transfusion, Hgb values collected within 4 weeks after transfusion were not included in the primary efficacy analysis. Change from Baseline = Hgb at Week 12 - Baseline Hgb. Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.	
End point type	Primary
End point timeframe: Baseline, Week 12	

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	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	10	6	
Units: grams/liter				
arithmetic mean (standard deviation)	35.6 (± 14.70)	32.5 (± 20.03)	-3.7 (± 15.77)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who had Transfusion Avoidance During 12 Weeks of Treatment With ALXN2050

End point title	Number of Participants who had Transfusion Avoidance During 12 Weeks of Treatment With ALXN2050
End point description: Transfusion avoidance: participants remained transfusion-free and did not require a transfusion during the period of interest. Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study.	
End point type	Secondary
End point timeframe: Baseline up to Week 12	

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	11	6	
Units: participants	9	10	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Red Blood Cell (RBC) Units Transfused During 12 Weeks of Treatment

End point title	Number of Red Blood Cell (RBC) Units Transfused During 12 Weeks of Treatment
End point description: Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study.	
End point type	Secondary
End point timeframe: Baseline up to Week 12	

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	11	6	
Units: RBC units				
arithmetic mean (standard deviation)	0.6 (\pm 1.24)	0.1 (\pm 0.30)	0.8 (\pm 2.04)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Transfusion Instances During 12 Weeks of Treatment

End point title	Number of Transfusion Instances During 12 Weeks of Treatment
End point description: Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study.	
End point type	Secondary
End point timeframe: Baseline up to Week 12	

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	11	6	
Units: transfusion instances				
arithmetic mean (standard deviation)	0.4 (\pm 0.90)	0.1 (\pm 0.30)	0.5 (\pm 1.22)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Lactate Dehydrogenase (LDH) at Week 12

End point title	Change From Baseline in Lactate Dehydrogenase (LDH) at Week 12
End point description: Change from Baseline = Serum LDH levels at Week 12 - Baseline Serum LDH levels. Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.	
End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	6	
Units: units/liter				
arithmetic mean (standard deviation)	-1310.8 (± 424.89)	160.2 (± 279.57)	88.7 (± 265.00)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Direct and Total Bilirubin at Week 12

End point title	Change From Baseline in Direct and Total Bilirubin at Week 12
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End point description:

Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure. 'Number analyzed' = participants evaluable for the specified category.

End point type	Secondary
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End point timeframe:

Baseline, Week 12

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	6	
Units: micromoles (μmol)/liter				
arithmetic mean (standard deviation)				
Direct Bilirubin	-2.1 (± 2.10)	-6.3 (± 5.16)	0.4 (± 0.89)	
Total Bilirubin	-12.9 (± 10.07)	-23.3 (± 24.89)	1.5 (± 2.81)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Absolute Reticulocyte Count at Week 12

End point title	Change From Baseline in Absolute Reticulocyte Count at Week 12
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End point description:

Change from Baseline = absolute reticulocyte count at Week 12 - Baseline reticulocyte count. Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, Week 12

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	10	5	
Units: 10 ³ cells/microliter (μL)				
arithmetic mean (standard deviation)	-100.6 (± 72.18)	-179.0 (± 117.30)	-24.0 (± 22.10)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Paroxysmal Nocturnal Hemoglobinuria (PNH) Red Blood Cell (RBC) Clone Size at Week 12

End point title	Change From Baseline in Paroxysmal Nocturnal Hemoglobinuria (PNH) Red Blood Cell (RBC) Clone Size at Week 12
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End point description:

The PNH RBC clone size refers to the percentage of PNH-affected cells versus normal cells within the total cell population. Change from Baseline = PNH clone size at Week 12 - Baseline PNH clone size. Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, Week 12

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	3	2	
Units: percentage of the total cell population				
arithmetic mean (standard deviation)	41.9 (± 13.68)	27.5 (± 21.60)	-12.0 (± 26.94)	

Statistical analyses

Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Events Leading to Discontinuation of Study Medication

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Events Leading to Discontinuation of Study Medication
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End point description:

An adverse event (AE) was 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, resulted in persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions, congenital anomaly/birth defect, or an important medical event or reaction. A TEAE was defined as an AE that emerged during treatment, had been absent prior to treatment, or worsened relative to the pretreatment state. A summary of all SAEs and Other Adverse Events (nonserious) regardless of causality is located in the 'Reported Adverse Events' Section. Safety set included all participants who received at least 1 dose of ALXN2050 in this study.

End point type	Secondary
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End point timeframe:

From first dose of study drug up to Week 217

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	11	6	
Units: participants				
Any AEs	12	10	6	
SAEs	7	5	2	
AEs Leading to Discontinuation of Study Medication	1	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Component 3 (C3) Fragment Deposition on PNH RBCs at Week 12

End point title	Change From Baseline in Component 3 (C3) Fragment Deposition on PNH RBCs at Week 12
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End point description:

C3 fragment deposition on PNH RBC was used as a marker of intra and extravascular hemolysis. Data are presented for the change from baseline to Week 12 in percentage of PNH RBCs with C3 fragment deposition. Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, Week 12

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	3	2	
Units: percentage of PNH RBC				
arithmetic mean (standard deviation)	0.0 (\pm 0.00)	-388.6 (\pm 590.08)	0.3 (\pm 0.35)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hgb at the End of Treatment (EOT) During the LTE Period

End point title	Change From Baseline in Hgb at the End of Treatment (EOT) During the LTE Period
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End point description:

Hgb baseline was defined as the lowest Hgb value observed between and including screening and first dose date. Change from Baseline = Hgb at the EOT visit - Baseline Hgb. Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, EOT visit (Maximum exposure: 213.4 weeks)

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	8	5	
Units: grams/liter				
arithmetic mean (standard deviation)	44.9 (\pm 21.07)	32.5 (\pm 7.17)	2.4 (\pm 19.44)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in LDH at the EOT During the LTE Period

End point title	Change From Baseline in LDH at the EOT During the LTE Period
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End point description:

Change from Baseline = Serum LDH levels at the EOT visit - Baseline Serum LDH levels. Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study. Here, 'Overall number

of participants analyzed' = participants evaluable for this outcome measure.

End point type	Secondary
End point timeframe:	
Baseline, EOT visit (Maximum exposure: 213.4 weeks)	

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	10	5	
Units: units/liter				
arithmetic mean (standard deviation)	-1084.1 (\pm 738.26)	95.7 (\pm 223.88)	-61.4 (\pm 62.85)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale (Version 4) Total Score at Week 12

End point title	Change From Baseline in Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue Scale (Version 4) Total Score at Week 12
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End point description:

The FACIT-Fatigue scale is a collection of quality-of-life questionnaires pertaining to the management of fatigue symptoms due to chronic illness. The FACIT-Fatigue is a 13-item questionnaire that assesses self-reported fatigue and its impact upon daily activities and function over the preceding 7 days. Participants scored each item on a 5-point scale: 0 (Not at all) to 4 (Very much). Total scores ranged from 0 to 52, with higher score indicating better quality of life. Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.

End point type	Secondary
End point timeframe:	
Baseline, Week 12	

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	7	6	
Units: units on a scale				
arithmetic mean (standard deviation)	11.2 (\pm 13.20)	5.1 (\pm 8.47)	0.2 (\pm 3.13)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in FACIT-Fatigue Scale (Version 4) Total Score at the EOT During the LTE Period

End point title	Change From Baseline in FACIT-Fatigue Scale (Version 4) Total Score at the EOT During the LTE Period
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End point description:

The FACIT-Fatigue scale is a collection of quality-of-life questionnaires pertaining to the management of fatigue symptoms due to chronic illness. The FACIT-Fatigue is a 13-item questionnaire that assesses self-reported fatigue and its impact upon daily activities and function over the preceding 7 days. Participants scored each item on a 5-point scale: 0 (Not at all) to 4 (Very much). Total scores ranged from 0 to 52, with higher score indicating better quality of life. Full analysis set included all participants who received at least 1 dose of ALXN2050 in this study. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline, EOT visit (Maximum exposure: 213.4 weeks)

End point values	Group 1: Treatment Naive	Group 2: Eculizumab Switch	Group 3: Danicopan Rollover	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	9	5	
Units: units on a scale				
arithmetic mean (standard deviation)	12.6 (± 12.51)	4.4 (± 7.26)	-3.4 (± 10.26)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to Week 217

Adverse event reporting additional description:

Safety set included all participants who received at least 1 dose of ALXN2050 in this study.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	Group 1: Treatment Naive
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Reporting group description:

Participants who were treatment-naive received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.

Reporting group title	Group 3: Danicopan Rollover
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Reporting group description:

Participants who had received danicopan monotherapy during Study ACH471-103 (NCT03181633), switched to ALXN2050 in this study and received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.

Reporting group title	Group 2: Eculizumab Switch
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Reporting group description:

Participants who had received C5 inhibition with eculizumab for at least 6 months, who continued to experience anemia (Hgb <10 grams/dL) and reticulocytes above the ULN, switched to ALXN2050 in this study and received ALXN2050 orally for 12 weeks during the treatment period. At the end of Week 12, participants entered the 148-week LTE Period and continued to receive ALXN2050 orally.

Serious adverse events	Group 1: Treatment Naive	Group 3: Danicopan Rollover	Group 2: Eculizumab Switch
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	2 / 6 (33.33%)	5 / 11 (45.45%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Breakthrough haemolysis			
subjects affected / exposed	4 / 12 (33.33%)	1 / 6 (16.67%)	2 / 11 (18.18%)
occurrences causally related to treatment / all	0 / 5	1 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intravascular haemolysis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolysis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 12 (25.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobinuria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscle spasms			

subjects affected / exposed	3 / 12 (25.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Group 1: Treatment Naive	Group 3: Danicopan Rollover	Group 2: Eculizumab Switch
Total subjects affected by non-serious adverse events subjects affected / exposed	12 / 12 (100.00%)	6 / 6 (100.00%)	10 / 11 (90.91%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Lipoma subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Vascular disorders Hypertension subjects affected / exposed occurrences (all) Flushing subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1 1 / 12 (8.33%) 1	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	0 / 11 (0.00%) 0 0 / 11 (0.00%) 0
General disorders and administration site conditions Chest pain subjects affected / exposed occurrences (all) Chills subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all) Vaccination site pain subjects affected / exposed occurrences (all) Catheter site rash subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 6 / 12 (50.00%) 6 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0	1 / 6 (16.67%) 1 0 / 6 (0.00%) 0 3 / 6 (50.00%) 3 2 / 6 (33.33%) 2 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 1 / 6 (16.67%) 1	0 / 11 (0.00%) 0 2 / 11 (18.18%) 3 1 / 11 (9.09%) 1 2 / 11 (18.18%) 8 1 / 11 (9.09%) 1 1 / 11 (9.09%) 1 0 / 11 (0.00%) 0

Chest discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
General physical health deterioration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hyperthermia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Malaise			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	3
Non-cardiac chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	2 / 12 (16.67%)	2 / 6 (33.33%)	2 / 11 (18.18%)
occurrences (all)	2	2	2
Rebound effect			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nipple pain			

subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 12 (0.00%)	2 / 6 (33.33%)	1 / 11 (9.09%)
occurrences (all)	0	2	1
Atelectasis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dysphonia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Haemoptysis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypoxia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Pleural effusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract irritation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Psychiatric disorders			

Sleep disorder			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Anxiety			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	2 / 11 (18.18%)
occurrences (all)	0	2	2
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Insomnia			
subjects affected / exposed	3 / 12 (25.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Investigations			
Liver function test increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	3 / 11 (27.27%)
occurrences (all)	0	1	4
Blood creatine increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	2
Alanine aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	3 / 11 (27.27%)
occurrences (all)	0	0	4

Cardiac murmur			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Epstein-Barr virus antibody positive			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Low density lipoprotein increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Troponin increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Free haemoglobin present			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1

Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Ankle fracture			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Foot fracture			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Immunisation reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Joint dislocation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Radius fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Scar			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Skin abrasion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Tendon injury			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Transfusion reaction			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Upper limb fracture			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 11 (9.09%) 1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 12 (50.00%)	1 / 6 (16.67%)	3 / 11 (27.27%)
occurrences (all)	13	2	6
Taste disorder			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	4
Memory impairment			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Disturbance in attention			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 12 (8.33%)	2 / 6 (33.33%)	2 / 11 (18.18%)
occurrences (all)	1	2	2
Hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Restless legs syndrome			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			

Neutropenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Iron deficiency anaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Anaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	1	0	11
Haemolysis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	4 / 11 (36.36%)
occurrences (all)	0	0	10
Breakthrough haemolysis			
subjects affected / exposed	3 / 12 (25.00%)	1 / 6 (16.67%)	2 / 11 (18.18%)
occurrences (all)	5	1	3
Aplastic anaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Haemolytic anaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Intravascular haemolysis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Eye disorders			
Episcleritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cataract			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Conjunctival hyperaemia			

subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Exudative retinopathy			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Retinal degeneration			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Vitreous floaters			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	9	0	0
Abdominal pain			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	4	0	4
Vomiting			
subjects affected / exposed	4 / 12 (33.33%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	5	0	4
Toothache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Tongue geographic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Pancreatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Enteritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0

Dyspepsia			
subjects affected / exposed	3 / 12 (25.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	4	0	1
Diarrhoea			
subjects affected / exposed	2 / 12 (16.67%)	1 / 6 (16.67%)	2 / 11 (18.18%)
occurrences (all)	3	1	2
Nausea			
subjects affected / exposed	4 / 12 (33.33%)	1 / 6 (16.67%)	2 / 11 (18.18%)
occurrences (all)	4	1	4
Large intestine polyp			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Chronic gastritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 12 (25.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Gingival hypertrophy			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0

Hiatus hernia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Mouth ulceration subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Hepatobiliary disorders			
Hypertransaminasaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 11 (9.09%) 1
Jaundice subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	2 / 11 (18.18%) 3
Autoimmune hepatitis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 11 (9.09%) 1
Cholelithiasis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 11 (9.09%) 1
Hepatic steatosis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Skin and subcutaneous tissue disorders			
Rash pruritic subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 11 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 11 (9.09%) 1
Night sweats subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	1 / 11 (9.09%) 1
Pruritus subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Ecchymosis			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 11 (0.00%) 0
Erythema subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Rash maculo-papular subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Yellow skin subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Renal and urinary disorders			
Renal impairment subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 11 (0.00%) 0
Haemoglobinuria subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 6	0 / 6 (0.00%) 0	2 / 11 (18.18%) 4
Haematuria subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 5	2 / 6 (33.33%) 2	4 / 11 (36.36%) 5
Chromaturia subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	2 / 6 (33.33%) 4	1 / 11 (9.09%) 1
Acute kidney injury subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	1 / 11 (9.09%) 1
Dysuria subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 11 (0.00%) 0
Choluria subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 11 (9.09%) 1
Endocrine disorders			
Hypothyroidism			

subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	1	1	1
Muscle twitching			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	1 / 12 (8.33%)	2 / 6 (33.33%)	4 / 11 (36.36%)
occurrences (all)	2	3	7
Fibromyalgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Arthralgia			
subjects affected / exposed	5 / 12 (41.67%)	1 / 6 (16.67%)	4 / 11 (36.36%)
occurrences (all)	6	1	5
Arthritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	3 / 12 (25.00%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	3	0	0
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Rotator cuff syndrome			

subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Tendonitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Otitis media			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	2 / 11 (18.18%)
occurrences (all)	0	0	2
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	1 / 11 (9.09%)
occurrences (all)	0	1	2
Bacterial infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pulpitis dental			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	2 / 12 (16.67%)	1 / 6 (16.67%)	2 / 11 (18.18%)
occurrences (all)	2	1	2
Tinea cruris			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	3
Rhinitis			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	1	1	0
Abscess limb			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0

Tinea pedis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Ear infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Furuncle			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0
Gastroenteritis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	2	0	1
Influenza			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Onychomycosis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Pyelonephritis acute			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	4 / 12 (33.33%)	3 / 6 (50.00%)	2 / 11 (18.18%)
occurrences (all)	5	3	2
Tinea versicolour			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	6 / 12 (50.00%)	2 / 6 (33.33%)	1 / 11 (9.09%)
occurrences (all)	10	3	1
Metabolism and nutrition disorders			
Vitamin B12 deficiency			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Iron deficiency			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Hyperlipidaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypervolaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			

subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Hypophagia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	0 / 11 (0.00%)
occurrences (all)	2	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 April 2020	This global amendment was initiated to allow females of childbearing potential to participate in the study and to align the protocol with Alexion standards in all applicable sections. The changes include updates to the eligibility criteria, SAE reporting, list of protocol-specific laboratory assessments, vaccination requirements, and the statistical sections. The Schedule of Activities was updated to reflect these changes.
07 January 2021	This global amendment was initiated to align the participant population of this Phase 2 study with the expected Phase 3 populations and to explore the efficacy and safety of ALXN2050 as a monotherapy option for participants with PNH. The changes include updates to the study design, eligibility criteria, and clarification of the endpoints. Changes were also made to further align the protocol with Alexion standards in all applicable sections, including SAE reporting, list of protocol-specific laboratory assessments, vaccination requirements, and other safety monitoring and the statistical sections. The Schedule of Activities was updated to reflect these changes.
12 April 2021	This global amendment was initiated to add back an exclusion criterion regarding history or presence of any risk factors for Torsades de Pointes, a screening QTcF interval > 450 milliseconds (msec) for males and > 470 msec for females, or receiving medications known to significantly increase QTc interval, which was inadvertently removed from Protocol Amendment 2.0.
03 May 2021	This global amendment was initiated to remove the following language from the dose-escalation instructions: "Dose escalation to 180 mg bid will be allowed once additional safety data from the currently ongoing Study ALXN2050-HV-107 is available. The Sponsor will inform study sites when dose escalation can be implemented." Preliminary data from Study ALXN2050-HV-107 were now available to support the dose escalation to proceed. This amendment also included additional information regarding prohibited medications (that is, list of inhibitors, inducers, and substrates of cytochrome P3A [CYP3A], and list of medications known to lower seizure threshold).
07 October 2021	This global amendment was initiated to extend the LTE Period for an additional 52 weeks to collect safety and efficacy data for longer term. This amendment also included: <ul style="list-style-type: none">• Clarification of exclusion criteria and additional prohibited medications to align with exclusion criteria.• Changes implemented in response to questions from the regulatory body in Germany (Protocol Amendment 3.2).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported