Clinical trial results:
A Randomized, Open-label Eculizumab and Ravulizumab Controlled, Non-Inferiority Study to Evaluate the Efficacy and Safety of Pozelimab and Cemdisiran Combination Therapy in Patients with Paroxysmal Nocturnal Hemoglobinuria who are Currently Treated with Eculizumab or Ravulizumab

Summary

EudraCT number	2020-002761-33
Trial protocol	IT DE ES FR PL GR
Global end of trial date	12 July 2023

Results information

Result version number	v1 (current)
This version publication date	25 July 2024
First version publication date	25 July 2024

Trial information

Trial identification

Sponsor protocol code	R3918-PNH-2022

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05131204
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, NY, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	
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	12 July 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 July 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was:

To evaluate the effect of pozelimab and cemdisiran combination therapy on hemolysis, as assessed by lactate dehydrogenase (LDH), after 36 weeks of treatment, in participants with PNH who switch from eculizumab or ravulizumab therapy versus participants who continue their eculizumab or ravulizumab therapy.

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the ICH guidelines for GCP and applicable regulatory requirements.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	06 October 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Philippines: 1
Worldwide total number of subjects	3
EEA total number of subjects	1

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)	3
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 140 participants were expected to be enrolled, however, due to feasibility: five participants were screened and 3 were randomized and treated. There were 2 screen failures.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pozelimab and Cemdisiran

Arm description:

Randomized 1:1

Arm type	Experimental
Investigational medicinal product name	Pozelimab
Investigational medicinal product code	R3918
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Intravenous use

Dosage and administration details:

Administered per protocol

Investigational medicinal product name	Ravulizumab
Investigational medicinal product code	ALXN1210
Other name	Ultomiris
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Intravenous use

Dosage and administration details:

Administered per protocol

Investigational medicinal product name	Eculizumab
Investigational medicinal product code	
Other name	Soliris
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Intravenous use

Dosage and administration details:

Administered per protocol

Investigational medicinal product name	Cemdisiran
Investigational medicinal product code	ALN-CC5
Other name	
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered per protocol

Arm title	Anti-C5 standard-of-care

Arm description: Randomized 1:1	
Arm type	Experimental
Investigational medicinal product name	Ravulizumab
Investigational medicinal product code	ALXN1210
Other name	Ultomiris
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Intravenous use
Dosage and administration details: Administered per protocol	
Investigational medicinal product name	Eculizumab
Investigational medicinal product code	
Other name	Soliris
Pharmaceutical forms	Cutaneous liquid
Routes of administration	Intravenous use
Dosage and administration details: Administered per protocol	

Number of subjects in period 1	Pozelimab and Cemdisiran	Anti-C5 standard-of-care
Started	2	1
Completed	0	0
Not completed	2	1
Sponsor decision	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Pozelimab and Cemdisiran
Reporting group description:	
Randomized 1:1	
Reporting group title	Anti-C5 standard-of-care
Reporting group description:	
Randomized 1:1	

Reporting group values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care	Total
Number of subjects	2	1	3
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	1	3
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender Categorical Units: Subjects			
Female	1	0	1
Male	1	1	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	1	0	1
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	2	1	3
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Pozelimab and Cemdisiran
Reporting group description: Randomized 1:1	
Reporting group title	Anti-C5 standard-of-care
Reporting group description: Randomized 1:1	

Primary: Percent change in lactate dehydrogenase (LDH) from baseline to week 36

End point title	Percent change in lactate dehydrogenase (LDH) from baseline to week 36[1]
End point description:	
End point type	Primary
End point timeframe: Baseline to week 36	

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: No data was collected so no statistical analysis was completed.

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Percentage of change				
number (not applicable)				

Notes:

[2] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[3] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with transfusion avoidance after day 1 through week 36

End point title	Percentage of participants with transfusion avoidance after day 1 through week 36
End point description:	
End point type	Secondary
End point timeframe: Day 1 through week 36	

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: Percentage				
number (not applicable)				

Notes:

[4] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[5] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with transfusion avoidance from week 4 through week 36

End point title	Percentage of participants with transfusion avoidance from week 4 through week 36

End point description:

End point type	Secondary

End point timeframe:

Week 4 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: Percentage				
number (not applicable)				

Notes:

[6] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[7] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with breakthrough hemolysis after day 1 through week 36

End point title	Percentage of participants with breakthrough hemolysis after day 1 through week 36

End point description:

End point type	Secondary

End point timeframe:

Day 1 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: Percentage				

Notes:

[8] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[9] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with hemoglobin stabilization after day 1 through week 36

End point title	Percentage of participants with hemoglobin stabilization after day 1 through week 36

End point description:

End point type	Secondary

End point timeframe:

Day 1 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: Percentage				

Notes:

[10] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[11] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with breakthrough hemolysis from week 4 through week 36

End point title	Percentage of participants with breakthrough hemolysis from week 4 through week 36

End point description:

End point type	Secondary

End point timeframe:
Week 4 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[12]	0[13]		
Units: Percentage				

Notes:
[12] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.
[13] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with hemoglobin stabilization from week 4 through week 36

End point title	Percentage of participants with hemoglobin stabilization from week 4 through week 36

End point description:

End point type	Secondary

End point timeframe:
Week 4 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[14]	0[15]		
Units: Percentage				

Notes:
[14] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.
[15] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who maintained adequate control of hemolysis from week 8 through week 36

End point title	Percentage of participants who maintained adequate control of hemolysis from week 8 through week 36

End point description:

End point type	Secondary

End point timeframe:
Week 8 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[16]	0[17]		
Units: Percentage of participants				

Notes:
[16] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.
[17] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with adequate control of LDH after day 1 though week 36

End point title	Percentage of participants with adequate control of LDH after day 1 though week 36

End point description:

End point type	Secondary

End point timeframe:
Day 1 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[18]	0[19]		
Units: Percentage				

Notes:
[18] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.
[19] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with adequate control of LDH from week 8 through week 36

End point title	Percentage of participants with adequate control of LDH from week 8 through week 36

End point description:

End point type	Secondary

End point timeframe:
Week 8 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[20]	0[21]		
Units: Percentage				

Notes:
[20] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.
[21] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with normalization of LDH after day 1 through week 36

End point title	Percentage of participants with normalization of LDH after day 1 through week 36

End point description:

End point type	Secondary

End point timeframe:
Day 1 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[22]	0[23]		
Units: Percentage				

Notes:
[22] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.
[23] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with normalization of LDH from week 8 through week 36

End point title	Percentage of participants with normalization of LDH from week 8 through week 36

End point description:

End point type	Secondary

End point timeframe:
Week 8 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[24]	0[25]		
Units: Percentage				

Notes:
[24] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.
[25] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who maintained adequate control of hemolysis after day 1 through week 36

End point title	Percentage of participants who maintained adequate control of hemolysis after day 1 through week 36

End point description:

End point type	Secondary

End point timeframe:
After day 1 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[26]	0[27]		
Units: Percentage of participants				

Notes:
[26] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.
[27] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fatigue as measured by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Scale from Baseline to Week 36

End point title	Change in fatigue as measured by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Scale from Baseline to Week 36

End point description:

End point type	Secondary

End point timeframe:
Baseline to week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[28]	0[29]		
Units: Score on a scale				

Notes:
[28] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.
[29] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in global health status (GHS)/QoL scale score on the EORTC-QLQ-C30 from baseline to week 36

End point title	Change in global health status (GHS)/QoL scale score on the EORTC-QLQ-C30 from baseline to week 36

End point description:

End point type	Secondary

End point timeframe:
Baseline to week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[30]	0[31]		
Units: Score on a scale				

Notes:
[30] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.
[31] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Physical Function (PF) score on the European organization for research and treatment of cancer quality-of-Life questionnaire Core 30 Items (EORTC-QLQ-C30) from baseline to week 36

End point title	Change in Physical Function (PF) score on the European organization for research and treatment of cancer quality-of-Life questionnaire Core 30 Items (EORTC-QLQ-C30) from baseline to week 36

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[32]	0[33]		
Units: Score on a scale				

Notes:

[32] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[33] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of RBCs transfused per protocol algorithm after day 1 through week 36

End point title	Rate of RBCs transfused per protocol algorithm after day 1 through week 36

End point description:

End point type	Secondary

End point timeframe:

After day 1 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[34]	0[35]		
Units: Rate of transfusion				

Notes:

[34] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[35] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of RBCs transfused per protocol algorithm from week 4 through week 36

End point title	Rate of RBCs transfused per protocol algorithm from week 4 through week 36

End point description:

End point type	Secondary

End point timeframe:

Week 4 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[36]	0[37]		
Units: Rate of transfusion				

Notes:

[36] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[37] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of units of RBCs transfused per protocol algorithm after day 1 through week 36

End point title	Number of units of RBCs transfused per protocol algorithm after day 1 through week 36

End point description:

End point type	Secondary

End point timeframe:

After day 1 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[38]	0[39]		
Units: Number				

Notes:

[38] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[39] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of units of RBCs transfused per protocol algorithm from week 4 through week 36

End point title	Number of units of RBCs transfused per protocol algorithm from week 4 through week 36

End point description:

End point type	Secondary

End point timeframe:

Week 4 through week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[40]	0[41]		
Units: Number				

Notes:

[40] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[41] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in hemoglobin levels from baseline to week 36

End point title	Change in hemoglobin levels from baseline to week 36

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[42]	0[43]		
Units: Change				

Notes:

[42] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[43] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and severity of treatment emergent serious adverse events (SAEs) over 36 weeks

End point title	Incidence and severity of treatment emergent serious adverse events (SAEs) over 36 weeks

End point description:

End point type	Secondary

End point timeframe:

Over 36 weeks

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[44]	0[45]		
Units: Events				

Notes:

[44] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[45] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and severity of treatment-emergent adverse events (TEAEs) of special interest over 36 weeks

End point title	Incidence and severity of treatment-emergent adverse events (TEAEs) of special interest over 36 weeks

End point description:

End point type	Secondary

End point timeframe:

Over week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[46]	0[47]		
Units: Events				

Notes:

[46] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[47] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and severity TEAEs leading to treatment discontinuation over 36 weeks

End point title	Incidence and severity TEAEs leading to treatment discontinuation over 36 weeks

End point description:

End point type	Secondary

End point timeframe:
Over week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[48]	0[49]		
Units: Events				

Notes:
[48] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.
[49] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Change in total CH50 from baseline to week 36

End point title	Change in total CH50 from baseline to week 36

End point description:

End point type	Secondary

End point timeframe:
Baseline to week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[50]	0[51]		
Units: Units per milliliter (U/mL)				

Notes:
[50] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.
[51] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of total cemdisiran in plasma through week 32

End point title	Concentrations of total cemdisiran in plasma through week 32

End point description:

End point type	Secondary

End point timeframe:
Baseline through week 32

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[52]	0[53]		
Units: Concentration				

Notes:

[52] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[53] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of total pozelimab in serum through week 62

End point title	Concentrations of total pozelimab in serum through week 62

End point description:

End point type	Secondary

End point timeframe:

Baseline through week 62

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[54]	0[55]		
Units: Concentration				

Notes:

[54] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[55] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of total C5 in plasma through week 62

End point title	Concentration of total C5 in plasma through week 62

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 62

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[56]	0[57]		
Units: Concentration				

Notes:

[56] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[57] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in total CH50 from baseline to week 36

End point title	Percent change in total CH50 from baseline to week 36

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 36

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[58]	0[59]		
Units: Percentage of change				

Notes:

[58] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[59] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of total ravulizumab in plasma through week 44

End point title	Concentrations of total ravulizumab in plasma through week 44

End point description:

End point type	Secondary

End point timeframe:

Baseline through week 44

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[60]	0[61]		
Units: Concentration				

Notes:

[60] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[61] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of total eculizumab in serum through week 40

End point title	Concentrations of total eculizumab in serum through week 40

End point description:

End point type	Secondary

End point timeframe:

Baseline through week 40

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[62]	0[63]		
Units: Concentration				

Notes:

[62] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[63] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of treatment emergent anti-drug antibodies (ADAs) to pozelimab through week 62

End point title	Incidence of treatment emergent anti-drug antibodies (ADAs) to pozelimab through week 62

End point description:

End point type	Secondary

End point timeframe:

Baseline through week 62

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[64]	0[65]		
Units: ADAs				

Notes:

[64] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[65] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of treatment emergent ADAs to cemdisiran through week 62

End point title	Incidence of treatment emergent ADAs to cemdisiran through week 62

End point description:

End point type	Secondary

End point timeframe:

Baseline through week 62

End point values	Pozelimab and Cemdisiran	Anti-C5 standard-of-care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[66]	0[67]		
Units: ADAs				

Notes:

[66] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

[67] - Due to Early Termination, endpoint removed from Statistical Analysis Plan. Data not collected.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From first dose to week 29	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0
Reporting groups	
Reporting group title	Pozelimab Q4W and Cemdisiran
Reporting group description: Randomized 1:1	
Reporting group title	Anti-C5 standard-of-care
Reporting group description: Randomized 1:1	

Serious adverse events	Pozelimab Q4W and Cemdisiran	Anti-C5 standard-of-care	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 1 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Pozelimab Q4W and Cemdisiran	Anti-C5 standard-of-care	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	1 / 1 (100.00%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 2 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Blood glucose increased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Injection site rash subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1	0 / 1 (0.00%) 0	
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 1 (100.00%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 June 2022	Main purpose for this amendment was to include new secondary endpoints and provide details on the planned analyses.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

20Dec2022 - sponsor decided to terminate study due to feasability challenges related to enrollment. There were no safety or efficacy concerns.

Notes: