Clinical trial results:
A Randomized, Double-blind, Active-controlled, Phase 3 Study Evaluating the Efficacy and Safety of ABP 959 Compared With Eculizumab in Adult Subjects With Paroxysmal Nocturnal Hemoglobinuria (PNH)

Summary

EudraCT number	2017-001418-27
Trial protocol	DE ES NL GB CZ NO SI IE FI SE PT IT
Global end of trial date	12 July 2022

Results information

Result version number	v1 (current)
This version publication date	13 April 2023
First version publication date	13 April 2023

Trial information

Trial identification

Sponsor protocol code	20150168

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03818607
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States,
Public contact	Study Director, Amgen Inc., medinfo@amgen.com
Scientific contact	Study Director, Amgen Inc., medinfo@amgen.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	12 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of ABP 959 compared with that of eculizumab based on control of intravascular hemolysis.

Protection of trial subjects:

The study was conducted in accordance with the Note for Guidance on Good Clinical Practice (International Council for Harmonisation Guideline E6 [R1] and 21 Code of Federal Regulations Parts 50, 56, and 312), the general principles indicated in the Declaration of Helsinki, and all applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 January 2019
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	Italy: 9
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	Turkey: 3
Country: Number of subjects enrolled	Finland: 2
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Slovenia: 2
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	42
EEA total number of subjects	32

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)	30
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 25 research centers in 14 countries including the Czech Republic, Finland, France, Ireland, Italy, the Netherlands, Norway, Portugal, Slovenia, Spain, Sweden, Turkey, the United Kingdom, and the United States, and participated from 22 January 2019 to 12 July 2022

Pre-assignment

Screening details:

42 adult participants with PNH were enrolled and randomized in a 1:1 ratio to receive each investigational product (ABP 959 and eculizumab) in 1 of 2 treatment sequences. Randomization was stratified by red blood cell (RBC) transfusion received within the last 12 months before randomization. There was no washout between Periods 1 and 2.

Period 1

Period 1 title	Period 1 (Week 1 to Week 52)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	ABP 959/Eculizumab

Arm description:

Participants received ABP 959 900 mg administered intravenously (IV) every 14 ± 2 days for 52 weeks in Period 1 followed by eculizumab 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.

Arm type	Experimental
Investigational medicinal product name	ABP 959
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ABP 959 900 mg was administered IV every 14 ± 2 days for 52 weeks in Period 1.

Arm title	Eculizumab/ABP 959

Arm description:

Participants received eculizumab 900 mg administered IV every 14 ± 2 days for 52 weeks in Period 1 followed by ABP 959 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.

Arm type	Active comparator
Investigational medicinal product name	Eculizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eculizumab 900 mg was administered IV every 14 ± 2 days for 52 weeks in Period 1.

Number of subjects in period 1	ABP 959/Eculizumab	Eculizumab/ABP 959
Started	20	22
Participants treated	20	22
Completed	20	21
Not completed	0	1
Adverse event, non-fatal	-	1

Period 2	
Period 2 title	Period 2 (Week 53 to Week 79)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	ABP 959/Eculizumab

Arm description:

Participants received ABP 959 900 mg administered intravenously (IV) every 14 ± 2 days for 52 weeks in Period 1 followed by eculizumab 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.

Arm type	Active comparator
Investigational medicinal product name	Eculizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eculizumab 900 mg was administered IV every 14 ± 2 days for 26 weeks in Period 2

Arm title	Eculizumab/ABP 959

Arm description:

Participants received eculizumab 900 mg administered IV every 14 ± 2 days for 52 weeks in Period 1 followed by ABP 959 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.

Arm type	Experimental
Investigational medicinal product name	ABP 959
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ABP 959 900 mg was administered IV every 14 ± 2 days for 26 weeks in Period 2.

Number of subjects in period 2	ABP 959/Eculizumab	Eculizumab/ABP 959
Started	20	21
Participants treated	20	21
Completed	19	20
Not completed	1	1
Consent withdrawn by subject	1	-
Participant's personal needs	-	1

Baseline characteristics

Reporting groups	
Reporting group title	ABP 959/Eculizumab
Reporting group description:	
Participants received ABP 959 900 mg administered intravenously (IV) every 14 ± 2 days for 52 weeks in Period 1 followed by eculizumab 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.	
Reporting group title	Eculizumab/ABP 959
Reporting group description:	
Participants received eculizumab 900 mg administered IV every 14 ± 2 days for 52 weeks in Period 1 followed by ABP 959 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.	

Reporting group values	ABP 959/Eculizumab	Eculizumab/ABP 959	Total
Number of subjects	20	22	42
Age categorical Units: Subjects			
In Utero	0	0	0
Pre-term newborn - gestational age < 37 wk	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)	15	15	30
Elderly (From 65-84 years)	5	7	12
Elderly 85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	50.2	50.2	
standard deviation	± 16.73	± 16.90	-
Sex: Female, Male Units: Participants			
Female	11	11	22
Male	9	11	20
Race/Ethnicity, Customized Units: Subjects			
White	16	17	33
Asian	0	1	1
Not allowed to collect	4	4	8
RBC Transfusion Within 12 Months Before Randomization per Electronic Case Report Form (eCRF) Units: Subjects			
Yes	2	3	5
No	18	19	37
Mean Number of Packed RBC Units Received in Last 12 Months			
Number of units of packed RBCs that were transfused in the 12 months prior to enrollment.			
Units: Packed RBC Units			
arithmetic mean	1.5	1.7	

standard deviation	± 0.71	± 1.15	-

End points

End points reporting groups

Reporting group title	ABP 959/Eculizumab
Reporting group description:	
Participants received ABP 959 900 mg administered intravenously (IV) every 14 ± 2 days for 52 weeks in Period 1 followed by eculizumab 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.	
Reporting group title	Eculizumab/ABP 959
Reporting group description:	
Participants received eculizumab 900 mg administered IV every 14 ± 2 days for 52 weeks in Period 1 followed by ABP 959 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.	
Reporting group title	ABP 959/Eculizumab
Reporting group description:	
Participants received ABP 959 900 mg administered intravenously (IV) every 14 ± 2 days for 52 weeks in Period 1 followed by eculizumab 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.	
Reporting group title	Eculizumab/ABP 959
Reporting group description:	
Participants received eculizumab 900 mg administered IV every 14 ± 2 days for 52 weeks in Period 1 followed by ABP 959 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.	
Subject analysis set title	ABP 959
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants in the modified FAS who received ABP 959 900 mg in Period 1 (administered IV every 14 ± 2 days for 52 weeks) or ABP 959 900 mg in Period 2 (administered IV every 14 ± 2 days for 26 weeks).	
Subject analysis set title	Eculizumab
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants in the modified FAS who received eculizumab 900 mg in Period 1 (administered IV every 14 ± 2 days for 52 weeks) or eculizumab 900 mg in Period 2 (administered IV every 14 ± 2 days for 26 weeks).	
Subject analysis set title	ABP 959
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received ABP 959 900 mg in Period 1 (administered IV every 14 ± 2 days for 52 weeks) or ABP 900 mg in Period 2 (administered IV every 14 ± 2 days for 26 weeks).	
Subject analysis set title	Eculizumab
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received eculizumab 900 mg in Period 1 (administered IV every 14 ± 2 days for 52 weeks) or eculizumab 900 mg in Period 2 (administered IV every 14 ± 2 days for 26 weeks).	
Subject analysis set title	ABP 959
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants received ABP 959 900 mg administered IV every 14 ± 2 days for 52 weeks in Period 1.	
Subject analysis set title	Eculizumab
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants received eculizumab 900 mg administered IV every 14 ± 2 days for 52 weeks in Period 1.	
Subject analysis set title	ABP 959
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who received ABP 959 900 mg in Period 1 (administered IV every 14 ± 2 days for 52 weeks) or ABP 959 900 mg in Period 2 (administered IV every 14 ± 2 days for 26 weeks).	
Subject analysis set title	Eculizumab

Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants who received eculizumab 900 mg in Period 1 (administered IV every 14 ± 2 days for 52 weeks) or eculizumab 900 mg in Period 2 (administered IV every 14 ± 2 days for 26 weeks).	
Subject analysis set title	ABP 959/Eculizumab
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants received ABP 959 900 mg administered IV every 14 ± 2 days for 52 weeks in Period 1 followed by eculizumab 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.	
Subject analysis set title	Eculizumab/ABP 959
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants received eculizumab 900 mg administered IV every 14 ± 2 days for 52 weeks in Period 1 followed by ABP 959 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.	

Primary: LDH Level at Week 27 (Parallel Comparison)

End point title	LDH Level at Week 27 (Parallel Comparison)
End point description:	
The primary analysis for the parallel comparison was hemolysis as measured by LDH at Week 27 by initial treatment received (Period 1). The full analysis set (FAS) included all randomized participants.	
End point type	Primary
End point timeframe:	
Week 27	

End point values	ABP 959	Eculizumab		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	22		
Units: U/L				
least squares mean (confidence interval 95%)	205.69 (191.23 to 221.24)	193.53 (180.80 to 207.17)		

Statistical analyses

Statistical analysis title	Ratio of Week 27 LDH levels (ABP959/eculizumab)
Comparison groups	ABP 959 v Eculizumab
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Geometric LS mean ratio (GMR)
Point estimate	1.0628
Confidence interval	
level	Other: 97.5 %
sides	1-sided
upper limit	1.1576

Notes:

[1] - The clinical similarity of the Week 27 LDH between treatments was assessed by comparing the 1-sided 97.5% upper confidence interval (CI) limit for the geometric mean ratio of LDH at Week 27 between ABP 959 treatment and eculizumab treatment with a non-inferiority margin of 2.873.

Primary: Time-adjusted Area Under the Effect Curve (AUEC) of LDH (Crossover Comparison)

End point title	Time-adjusted Area Under the Effect Curve (AUEC) of LDH (Crossover Comparison)

End point description:

The primary analysis for the crossover comparison was hemolysis, as measured by the time-adjusted AUEC of LDH, according to treatment per randomized sequence regardless of treatment actually received.
The modified FAS included all randomized participants with an LDH-time profile evaluable for the time-adjusted AUEC, according to treatment per the randomized sequence regardless of treatment actually received.

End point type	Primary

End point timeframe:

From Week 13 to Week 27, from Week 39 to Week 53, and from Week 65 to Week 79

End point values	ABP 959	Eculizumab		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40	40		
Units: U*day/L/week				
least squares mean (confidence interval 95%)	1445.76 (1295.63 to 1613.28)	1473.44 (1321.86 to 1642.41)		

Statistical analyses

Statistical analysis title	Ratio of LDH levels (ABP 959/eculizumab)
Comparison groups	ABP 959 v Eculizumab
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other[2]
Parameter estimate	GMR
Point estimate	0.9812
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9403
upper limit	1.0239

Notes:

[2] - The clinical similarity of the AUEC between treatments was assessed by comparing 2-sided 90% CI for the GMR of the time-adjusted AUEC of LDH (Week 13 to Week 27, Week 39 to Week 53, and Week 65 to Week 79) between ABP 959 treatment and eculizumab treatment with a similarity margin of (0.77, 1.30).

Secondary: Mean Total Complement (50% Total Hemolytic Complement Activity [CH50])

End point title	Mean Total Complement (50% Total Hemolytic Complement

	Activity [CH50])

End point description:

Total complement (%) was measured in serum using an assay method and compared the total hemolytic complement activity to the lower limit of the normal human reference (LLN) of 58 U/mL for all CH50 values. The percent of LLN of CH50 at each time point was calculated as mean CH50 results/LLN x 100%.
Baseline was defined as the last non-missing assessment taken prior to the first dose of IP. Results are presented for participants in the FAS with data available at each time point. The FAS included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 27, Week 39, Week 53, Week 65, and Week 79

End point values	ABP 959/Eculizumab	Eculizumab/ABP 959		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	22		
Units: Percent of LLN for all CH50 values				
arithmetic mean (standard deviation)				
Baseline (N = 20; 22)	6.4 (± 13.48)	2.6 (± 4.11)		
Week 27 (N = 19; 21)	7.5 (± 16.68)	6.3 (± 12.25)		
Week 39 (N = 17; 21)	7.4 (± 23.80)	5.1 (± 10.36)		
Week 53 (N = 20; 21)	12.0 (± 34.29)	4.6 (± 6.84)		
Week 65 (N = 16; 18)	25.6 (± 65.27)	7.8 (± 11.37)		
Week 79 (N = 18; 20)	15.8 (± 35.65)	6.5 (± 12.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Total Hemoglobin Levels

End point title	Mean Total Hemoglobin Levels

End point description:

Baseline was defined as the last non-missing assessment taken prior to the first dose of IP. Results are presented for participants in the FAS with data available at each time point. The FAS included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 27, Week 39, Week 53, Week 65, and Week 79

End point values	ABP 959/Eculizumab	Eculizumab/ABP 959		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	22		
Units: g/L				
arithmetic mean (standard deviation)				
Baseline (N = 20; 21)	113.0 (± 15.03)	113.8 (± 16.09)		
Week 27 (N = 18; 20)	110.6 (± 15.19)	116.1 (± 16.08)		
Week 39 (N = 16; 20)	114.6 (± 14.12)	115.0 (± 15.39)		
Week 53 (N = 19; 21)	109.8 (± 15.17)	115.8 (± 15.20)		
Week 65 (N = 15; 18)	106.9 (± 17.74)	115.7 (± 18.36)		
Week 79 (N = 19; 20)	113.0 (± 16.78)	115.7 (± 16.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Serum-free Hemoglobin Levels

End point title	Mean Serum-free Hemoglobin Levels

End point description:

Baseline was defined as the last non-missing assessment taken prior to the first dose of IP. Results are presented for participants in the FAS with data available at each time point. The FAS included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 27, Week 39, Week 53, Week 65, and Week 79

End point values	ABP 959/Eculizumab	Eculizumab/ABP 959		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	22		
Units: mg/dL				
arithmetic mean (standard deviation)				
Baseline (N = 20; 22)	9.30 (± 26.960)	3.76 (± 2.758)		
Week 27 (N = 17; 21)	5.38 (± 14.839)	3.10 (± 2.920)		
Week 39 (N = 17; 21)	3.74 (± 5.093)	10.25 (± 27.926)		
Week 53 (N = 18; 21)	13.60 (± 33.793)	3.08 (± 2.529)		
Week 65 (N = 16; 18)	3.22 (± 2.249)	2.75 (± 2.077)		
Week 79 (N = 17; 15)	6.59 (± 10.232)	13.89 (± 41.634)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Haptoglobin Levels

End point title	Mean Haptoglobin Levels

End point description:

Baseline was defined as the last non-missing assessment taken prior to the first dose of IP. Results are presented for participants in the FAS with data available at each time point. The FAS included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 27, Week 39, Week 53, Week 65, and Week 79

End point values	ABP 959/Eculizumab	Eculizumab/ABP 959		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	22		
Units: g/L				
arithmetic mean (standard deviation)				
Baseline (N = 20; 22)	0.200 (± 0.2562)	0.286 (± 0.3714)		
Week 27 (N = 19; 21)	0.201 (± 0.2809)	0.300 (± 0.4153)		
Week 39 (N = 18; 21)	0.196 (± 0.3085)	0.301 (± 0.4266)		
Week 53 (N = 20; 21)	0.196 (± 0.2571)	0.383 (± 0.6550)		
Week 65 (N = 16; 18)	0.201 (± 0.2521)	0.466 (± 0.5624)		
Week 79 (N = 19; 20)	0.201 (± 0.2473)	0.335 (± 0.4744)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Bilirubin Levels

End point title	Mean Bilirubin Levels

End point description:

Baseline was defined as the last non-missing assessment taken prior to the first dose of IP. Results are presented for participants in the FAS with data available at each time point. The FAS included all

randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 27, Week 39, Week 53, Week 65, and Week 79

End point values	ABP 959/Eculizumab	Eculizumab/ABP 959		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	22		
Units: micromol/L				
arithmetic mean (standard deviation)				
Baseline (N = 20; 22)	23.63 (± 12.537)	21.12 (± 13.872)		
Week 27 (N = 19; 21)	28.69 (± 22.529)	24.30 (± 19.209)		
Week 39 (N = 18; 21)	24.08 (± 14.258)	24.15 (± 16.655)		
Week 53 (N = 20; 21)	25.76 (± 17.156)	21.32 (± 14.036)		
Week 65 (N = 16; 18)	24.51 (± 16.736)	20.02 (± 13.808)		
Week 79 (N = 19; 20)	23.73 (± 16.161)	23.15 (± 17.286)		

Statistical analyses

No statistical analyses for this end point

Secondary: Degree of Hemoglobinuria

End point title	Degree of Hemoglobinuria

End point description:

The degree of hemoglobinuria was categorized as negative, trace, small, moderate, and large based on the analysis of urine samples collected from each participant at the specified timepoints.
Baseline was defined as the last non-missing assessment taken prior to the first dose of IP. Data is presented for the number of urine samples assessed at each timepoint for the FAS which included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 27, Week 39, Week 53, Week 65, and Week 79

End point values	ABP 959/Eculizumab	Eculizumab/ABP 959		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	22		
Units: Participants				
Baseline: Negative (N = 20; 21)	17	21		
Baseline: Trace (N = 20; 21)	0	0		
Baseline: Small (N = 20; 21)	2	0		
Baseline: Moderate (N = 20; 21)	0	0		
Baseline: Large (N = 20; 21)	1	0		
Week 27: Negative (N = 19; 21)	17	20		
Week 27: Trace (N = 19; 21)	0	1		
Week 27: Small (N = 19; 21)	1	0		
Week 27: Moderate (N = 19; 21)	0	0		
Week 27: Large (N = 19; 21)	1	0		
Week 39: Negative (N= 17; 21)	16	20		
Week 39: Trace (N= 17; 21)	1	1		
Week 39: Small (N= 17; 21)	0	0		
Week 39: Moderate (N= 17; 21)	0	0		
Week 39: Large (N= 17; 21)	0	0		
Week 53: Negative (N = 19; 20)	16	19		
Week 53: Trace (N = 19; 20)	1	1		
Week 53: Small (N = 19; 20)	1	0		
Week 53: Moderate (N = 19; 20)	1	0		
Week 53: Large (N = 19; 20)	0	0		
Week 65: Negative (N =16; 18)	15	17		
Week 65: Trace (N =16; 18)	0	1		
Week 65: Small (N = 16; 18)	0	0		
Week 65: Moderate (N = 16; 18)	0	0		
Week 65: Large (N = 16; 18)	1	0		
Week 79: Negative (N = 18; 20)	16	19		
Week 79: Trace (N = 18; 20)	0	1		
Week 79: Small (N = 18; 20)	1	0		
Week 79: Moderate (N = 18; 20)	0	0		
Week 79: Large (N = 18; 20)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage of Type III Erythrocytes

End point title	Mean Percentage of Type III Erythrocytes

End point description:

As a measure of hemolysis the mean percentage of Type III erythrocytes was measured at the specified timepoints.
Baseline was defined as the last non-missing assessment taken prior to the first dose of IP. Results are presented for participants in the FAS with data available at each time point. The FAS included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 27, Week 39, Week 53, Week 65 and Week 79

End point values	ABP 959/Eculizumab	Eculizumab/ABP 959		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	22		
Units: Percentage of Type III Erythrocytes				
arithmetic mean (standard deviation)				
Baseline (N = 18; 21)	39.9197 (± 25.36275)	36.7478 (± 29.93810)		
Week 27 (N = 17; 21)	40.9121 (± 23.17684)	40.1304 (± 30.01551)		
Week 39 (N = 16; 20)	41.2158 (± 24.81071)	43.3663 (± 29.65777)		
Week 53 (N = 19; 21)	41.8196 (± 23.23819)	40.4676 (± 31.14150)		
Week 65 (N = 15; 17)	39.1192 (± 22.20104)	37.5379 (± 28.76642)		
Week 79 (N = 15; 16)	43.7609 (± 21.51712)	42.5501 (± 30.20582)		

Statistical analyses

No statistical analyses for this end point

Secondary: LDH Levels at Week 53 and Week 79

End point title	LDH Levels at Week 53 and Week 79

End point description:

The analysis of the crossover comparison of hemolysis, as measured by LDH at Week 53 and Week 79. Results are presented for participants in the FAS with data available at each time point. The FAS included all randomized participants.

End point type	Secondary

End point timeframe:

Week 53 (first week of Period 2) and Week 79 (last week of Period 2)

End point values	ABP 959	Eculizumab		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	39	40		
Units: U/L				
least squares mean (confidence interval 95%)	209.95 (183.817 to 239.802)	203.56 (178.387 to 232.295)		

Statistical analyses

Statistical analysis title	GMR (ABP 959/Eculizumab)
Comparison groups	ABP 959 v Eculizumab
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	1.0314
Confidence interval	
level	Other: 97.5 %
sides	1-sided
upper limit	1.1201

Secondary: Mean LDH Levels by Visit up to Week 79

End point title	Mean LDH Levels by Visit up to Week 79

End point description:

Baseline was defined as the last non-missing assessment taken prior to the first dose of IP. Results are presented for participants in the FAS with data available at each time point. The FAS included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 3, Week 7, Week 13, Week 15, Week 19, Week 25, Week 27, Week 29, Week 33, Week 39, Week 41, Week 43, Week 45, Week 47, Week 49, Week 51, Week 53, Week 55, Week 59, Week 65, Week 67, Week 69, Week 71, Week 73, Week 75, Week 77, and Week 79

End point values	ABP 959/Eculizumab	Eculizumab/ABP 959		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	22		
Units: U/L				
arithmetic mean (standard deviation)				
Baseline (N = 20; 22)	199.7 (± 61.06)	193.9 (± 45.09)		
Week 3 (N = 19; 20)	210.7 (± 77.80)	185.8 (± 42.22)		
Week 7 (N = 19; 21)	201.4 (± 48.41)	194.0 (± 38.33)		
Week 13 (N = 18; 21)	207.7 (± 76.14)	206.2 (± 63.82)		
Week 15 (N = 17; 22)	213.4 (± 105.86)	197.0 (± 55.63)		

Week 19 (N = 19; 21)	188.5 (± 27.58)	201.0 (± 59.21)		
Week 25 (N = 18; 21)	230.5 (± 76.07)	190.2 (± 46.91)		
Week 27 (N = 18; 20)	191.7 (± 35.99)	192.2 (± 63.83)		
Week 29 (N = 19; 21)	207.2 (± 50.35)	202.1 (± 58.46)		
Week 33 (N = 17; 20)	194.6 (± 29.36)	206.8 (± 59.44)		
Week 39 (N = 18; 21)	188.1 (± 37.55)	196.9 (± 66.73)		
Week 41 (N = 19; 21)	196.1 (± 49.21)	199.7 (± 51.00)		
Week 43 (N = 18; 21)	215.9 (± 62.41)	207.1 (± 79.95)		
Week 45 (N = 19; 21)	202.8 (± 53.15)	199.4 (± 66.14)		
Week 47 (N = 19; 20)	199.4 (± 51.72)	197.6 (± 65.25)		
Week 49 (N = 19; 21)	216.2 (± 111.26)	203.2 (± 68.65)		
Week 51 (N = 19; 21)	229.9 (± 125.47)	197.7 (± 57.02)		
Week 53 (N = 20; 21)	224.0 (± 64.49)	184.7 (± 46.32)		
Week 55 (N = 18; 19)	213.9 (± 103.58)	188.0 (± 48.91)		
Week 59 (N = 19; 18)	209.4 (± 98.42)	191.4 (± 79.01)		
Week 65 (N = 16; 18)	230.6 (± 135.26)	180.9 (± 55.50)		
Week 67 (N = 19; 17)	196.1 (± 40.61)	186.2 (± 50.57)		
Week 69 (N = 19; 17)	200.1 (± 38.12)	186.2 (± 38.48)		
Week 71 (N = 18; 18)	196.8 (± 36.36)	186.6 (± 48.02)		
Week 73 (N = 19; 19)	210.3 (± 43.90)	181.9 (± 49.31)		
Week 75 (N = 17; 19)	207.9 (± 67.51)	191.4 (± 65.08)		
Week 77 (N = 14; 20)	209.6 (± 54.35)	181.4 (± 38.72)		
Week 79 (N = 19; 19)	229.2 (± 116.85)	185.8 (± 45.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean number of packed RBC Units Transfused per Month

End point title	Mean number of packed RBC Units Transfused per Month

End point description:

Baseline was defined as the last non-missing assessment taken prior to the first dose of IP. Results are presented for participants in the FAS who had packed RBC units transfused. The FAS included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline to End of Study (up to Week 79)

End point values	ABP 959/Eculizumab	Eculizumab/ABP 959		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2	6		
Units: packed RBC units per month				
arithmetic mean (standard deviation)	0.200 (± 0.1980)	0.238 (± 0.2078)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total and Unbound Pharmacokinetics (PK) Area Under the Curve (AUC) of ABP 959 and Eculizumab From Week 13 to Week 15 (Period 1)

End point title	Total and Unbound Pharmacokinetics (PK) Area Under the Curve (AUC) of ABP 959 and Eculizumab From Week 13 to Week 15 (Period 1)

End point description:

The total and unbound PK concentration AUC values from Week 13 to Week 15 in Period 1 are presented by actual treatment received.
The PK parameter analysis set consisted of a subset of participants from the safety analysis set with an evaluable ABP 959 or eculizumab serum concentration time profile from Week 13 to Week 15

End point type	Secondary

End point timeframe:

PK samples were collected predose and immediately postdose Week 13, 7 days post the Week 13 dose (Week 14), and predose at Week 15

End point values	ABP 959	Eculizumab		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	19		
Units: µg*day/mL				
geometric mean (geometric coefficient of variation)				
Total PK AUC	3898.05 (± 37.5)	4273.28 (± 30.6)		
Unbound PK AUC	2761.19 (± 51.3)	2903.93 (± 40.6)		

Statistical analyses

Statistical analysis title	Unbound PK AUC GMR (ABP 959/Eculizumab)
Comparison groups	ABP 959 v Eculizumab
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMR
Point estimate	0.9508
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7454
upper limit	1.213

Statistical analysis title	Total PK AUC GMR (ABP 959/Eculizumab)
Comparison groups	ABP 959 v Eculizumab
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMR
Point estimate	0.9122
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7586
upper limit	1.0968

Secondary: Total and Unbound Trough Serum Concentrations of ABP 959 and Eculizumab

End point title	Total and Unbound Trough Serum Concentrations of ABP 959 and Eculizumab

End point description:

The total and unbound serum trough concentrations are presented by treatment sequence received for the prespecified time points. Baseline was defined as the last non-missing assessment taken prior to the first dose of IP.
The PK concentration analysis set consisted of a subset of participants from the safety analysis set with at least one serum concentration (including results below the quantifiable limit) of ABP 959 or eculizumab, with data analyzed according to actual treatment received. Participants with data available at each time point are presented.

End point type	Secondary

End point timeframe:

PK samples were collected predose at the prespecified timepoints: baseline, Week 3, Week 7, Week 13, Week 15, Week 19, Week 27, Week 33, Week 39, Week 45, Week 51, Week 53, Week 55, Week 59, Week 65, Week 71, Week 77, and Week 79

End point values	ABP 959/Eculizumab	Eculizumab/ABP 959		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	22		
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Baseline: Total (N = 20; 22)	200.15 (± 52.8)	202.58 (± 44.3)		
Baseline: Unbound (N = 20; 22)	94.62 (± 100.1)	117.48 (± 71.5)		
Week 3: Total (N = 20; 21)	205.25 (± 48.8)	197.67 (± 42.9)		
Week 3: Unbound (N = 20; 21)	113.99 (± 91.5)	116.87 (± 68.9)		
Week 7: Total (N = 20; 20)	213.51 (± 50.1)	194.80 (± 42.5)		
Week 7: Unbound (N = 20; 20)	116.57 (± 92.1)	98.34 (± 108.9)		
Week 13: Total (N = 20; 21)	215.54 (± 55.8)	201.60 (± 45.6)		
Week 13: Unbound (N = 20; 21)	114.40 (± 98.4)	123.73 (± 69.1)		
Week 15: Total (N = 18; 21)	192.80 (± 49.1)	205.07 (± 36.9)		
Week 15: Unbound (N = 18; 21)	98.68 (± 87.0)	123.11 (± 66.1)		
Week 19: Total (N = 19; 21)	216.46 (± 46.3)	200.51 (± 49.1)		
Week 19: Unbound (N = 19; 21)	133.39 (± 75.2)	120.54 (± 77.3)		
Week 25: Total (N = 18; 21)	217.75 (± 50.2)	200.59 (± 51.7)		
Week 25: Unbound (N = 18; 21)	134.37 (± 95.5)	112.73 (± 96.4)		
Week 27: Total (N = 19; 21)	198.17 (± 58.9)	203.19 (± 45.3)		
Week 27: Unbound (N = 19; 21)	112.02 (± 111.0)	122.00 (± 83.8)		
Week 33: Total (N = 17; 21)	211.62 (± 55.5)	196.57 (± 49.1)		
Week 33: Unbound (N = 17; 21)	130.12 (± 117.3)	126.36 (± 78.4)		
Week 39: Total (N = 17; 21)	183.57 (± 68.3)	201.47 (± 48.1)		
Week 39: Unbound (N = 17; 21)	131.50 (± 104.8)	129.89 (± 75.1)		
Week 45: Total (N = 18; 21)	204.62 (± 52.7)	197.67 (± 47.9)		
Week 45: Unbound (N = 18; 21)	130.30 (± 92.0)	126.36 (± 77.3)		
Week 51: Total (N = 18; 21)	207.20 (± 59.6)	200.41 (± 45.5)		
Week 51: Unbound (N = 18; 21)	130.32 (± 117.4)	123.27 (± 68.3)		
Week 53: Total (N = 20; 21)	193.77 (± 54.4)	198.89 (± 46.3)		
Week 53: Unbound (N = 20; 21)	108.40 (± 130.3)	124.82 (± 74.6)		
Week 55: Total (N = 19; 20)	210.22 (± 59.0)	185.34 (± 48.4)		

Week 55: Unbound (N = 19; 20)	132.20 (± 125.4)	117.93 (± 77.2)		
Week 59: Total (N = 19; 20)	184.38 (± 58.9)	192.66 (± 46.6)		
Week 59: Unbound (N = 19; 20)	111.48 (± 121.5)	122.01 (± 78.5)		
Week 65: Total (N = 16; 18)	190.09 (± 62.0)	202.83 (± 51.5)		
Week 65: Unbound (N = 16; 18)	110.57 (± 146.9)	120.72 (± 87.7)		
Week 71: Total (N = 17; 16)	160.43 (± 99.5)	188.05 (± 58.6)		
Week 71: Unbound (N = 17; 16)	101.66 (± 156.7)	104.82 (± 115.0)		
Week 77: Total (N = 15; 17)	211.80 (± 47.2)	198.24 (± 54.8)		
Week 77: Unbound (N = 15; 17)	140.07 (± 98.3)	111.83 (± 99.8)		
Week 79: Total (N = 18; 20)	178.29 (± 60.7)	199.91 (± 50.0)		
Week 79: Unbound (N = 18; 20)	101.98 (± 133.1)	116.28 (± 96.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs)

End point description:

TEAEs are any adverse event (AE) that began or increased in severity or frequency at or after the time of first treatment up to end of study (up to Week 79). A treatment-emergent serious adverse event (SAE) was a TEAE that met at least 1 of the following criteria: was fatal, life-threatening, required or prolonged inpatient hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was another medically important serious event.
The treatment-emergent events of interest (EOI) prespecified for this study included serious infections (meningococcus aspergillus, and other serious infections/sepsis), and infusion reactions. The safety analysis set included all treated participants, with treatment assigned based on actual treatment received.

End point type	Secondary

End point timeframe:

Day 1 to End of Study (up to Week 79)

End point values	Eculizumab	ABP 959		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	42	41		
Units: Participants				
All TEAEs	39	33		
Any Treatment-emergent SAE	2	7		
Any Treatment-emergent EOI: Infusion reaction	15	15		

Any Treatment-emergent EOI: Serious infection	0	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Antidrug Antibodies (ADAs)

End point title	Number of Participants with Antidrug Antibodies (ADAs)

End point description:

Any samples that tested positive for binding antibodies were also tested for neutralizing antibodies. Treatment boosted ADAs were defined as a positive immunoassay result at baseline and at least 1 postbaseline immunoassay result that was ≥ 4 times the magnitude of the baseline result. Baseline was defined as the last non-missing assessment taken prior to the first dose of IP.
Ab = antibody; NAb = neutralizing antibody; +ve = positive; -ve = negative; BL = baseline

End point type	Secondary

End point timeframe:

Blood samples for ADA assessments were taken predose at baseline, Week 3, Week 7, Week 13, Week 19, Week 25, Week 27, Week 33, Week 39, Week 45, Week 51, Week 53, Week 55, Week 59, Week 65, Week 71, Week 77 and Week 79.

End point values	ABP 959/Eculizumab	Eculizumab/ABP 959		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	22		
Units: Participants				
Binding Ab +ve anytime	0	2		
NAb +ve anytime	0	0		
Binding Ab +ve at/before BL	0	0		
NAb +ve at/before BL	0	0		
Treatment boosted Ab +ve	0	0		
Binding Ab +ve post-BL with -ve/no result at BL	0	2		
NAb +ve post-BL with -ve/no result at BL	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to End of Study (up to Week 79)

Adverse event reporting additional description:

All-cause mortality is reported for all participants enrolled/randomized in the study. Serious adverse events and other adverse events are reported for all participants who received at least one dose of study drug.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Period 1: ABP 959

Reporting group description:

Participants received ABP 959 900 mg administered IV every 14 ± 2 days for 52 weeks in Period 1.

Reporting group title	Period 2: ABP 959

Reporting group description:

Participants received ABP 959 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.

Reporting group title	Period 2: Eculizumab

Reporting group description:

Participants received eculizumab 900 mg administered IV every 14 ± 2 days for 26 weeks in Period 2.

Reporting group title	Period 1: Eculizumab

Reporting group description:

Participants received eculizumab 900 mg administered IV every 14 ± 2 days for 52 weeks in Period 1.

Serious adverse events	Period 1: ABP 959	Period 2: ABP 959	Period 2: Eculizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)	4 / 21 (19.05%)	1 / 20 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	0 / 20 (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
Cardiac disorders			
Cardiac failure			

subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Vertigo CNS origin			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (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 / 20 (0.00%)	1 / 21 (4.76%)	0 / 20 (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

Serious adverse events	Period 1: Eculizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 22 (4.55%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure chronic			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Vertigo CNS origin			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Period 1: ABP 959	Period 2: ABP 959	Period 2: Eculizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 20 (75.00%)	17 / 21 (80.95%)	18 / 20 (90.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hypotension			

subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 21 (9.52%)	3 / 20 (15.00%)
occurrences (all)	0	2	4
Chills			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Catheter site pruritus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	2 / 20 (10.00%)	2 / 21 (9.52%)	1 / 20 (5.00%)
occurrences (all)	2	3	1
Influenza like illness			
subjects affected / exposed	2 / 20 (10.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	4	0	0
Pyrexia			
subjects affected / exposed	6 / 20 (30.00%)	3 / 21 (14.29%)	1 / 20 (5.00%)
occurrences (all)	9	4	2
Pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Vaginal discharge			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Intermenstrual bleeding			

subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Cough			
subjects affected / exposed	2 / 20 (10.00%)	2 / 21 (9.52%)	1 / 20 (5.00%)
occurrences (all)	2	2	1
Sinonasal obstruction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Vitamin D decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Weight increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Vaccination complication			

subjects affected / exposed	1 / 20 (5.00%)	2 / 21 (9.52%)	2 / 20 (10.00%)
occurrences (all)	1	2	2
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Vertigo CNS origin			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	3 / 20 (15.00%)	2 / 21 (9.52%)	1 / 20 (5.00%)
occurrences (all)	3	2	2
Dizziness			
subjects affected / exposed	2 / 20 (10.00%)	2 / 21 (9.52%)	0 / 20 (0.00%)
occurrences (all)	2	3	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 20 (20.00%)	3 / 21 (14.29%)	1 / 20 (5.00%)
occurrences (all)	5	3	1
Haemolysis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 21 (0.00%)	2 / 20 (10.00%)
occurrences (all)	3	0	5
Thrombocytopenia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 21 (9.52%)	0 / 20 (0.00%)
occurrences (all)	0	3	0
Neutropenia			
subjects affected / exposed	1 / 20 (5.00%)	2 / 21 (9.52%)	0 / 20 (0.00%)
occurrences (all)	2	3	0
Leukopenia			

subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye pruritus			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Neovascular age-related macular degeneration			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	3 / 20 (15.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	3	0	1
Dyspepsia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	3 / 20 (15.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	4	2	1
Abdominal pain upper			
subjects affected / exposed	0 / 20 (0.00%)	2 / 21 (9.52%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Abdominal distension			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Cholecystitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Ocular icterus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Hyperbilirubinaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	8	0	0
Skin and subcutaneous tissue disorders			
Rash pruritic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Pruritus			
subjects affected / exposed	2 / 20 (10.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	2	2	1
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	2
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Haemoglobinuria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Chromaturia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Bilirubinuria			

subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 20 (10.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	3	1	0
Arthritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	2 / 20 (10.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	2	2	1
Flank pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	2 / 20 (10.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Myalgia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Muscle fatigue			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Enterovirus infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Influenza			

subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Lyme disease			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	5 / 20 (25.00%)	4 / 21 (19.05%)	1 / 20 (5.00%)
occurrences (all)	8	4	1
Pharyngitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Conjunctivitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
COVID-19			
subjects affected / exposed	0 / 20 (0.00%)	3 / 21 (14.29%)	5 / 20 (25.00%)
occurrences (all)	0	3	5
Urinary tract infection			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Wound infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0

Vitamin B12 deficiency			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

Non-serious adverse events	Period 1: Eculizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 22 (90.91%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lipoma			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	5		
Flushing			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Chills			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Catheter site pruritus			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Influenza like illness			

subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Malaise			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Vaginal discharge			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Intermenstrual bleeding			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Sinonasal obstruction			

subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Vitamin D decreased			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	4		
Vaccination complication			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	6		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Vertigo CNS origin			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		

Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	 9 / 22 (40.91%) 11 2 / 22 (9.09%) 2		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Haemolysis subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all)	 4 / 22 (18.18%) 12 2 / 22 (9.09%) 3 2 / 22 (9.09%) 2 2 / 22 (9.09%) 2 0 / 22 (0.00%) 0		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	 2 / 22 (9.09%) 2		
Eye disorders Eye pruritus subjects affected / exposed occurrences (all) Neovascular age-related macular degeneration subjects affected / exposed occurrences (all)	 0 / 22 (0.00%) 0 0 / 22 (0.00%) 0		
Gastrointestinal disorders Haemorrhoids			

subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Cholecystitis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Ocular icterus			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash pruritic			

subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Eczema subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0 1 / 22 (4.55%) 2 2 / 22 (9.09%) 2 1 / 22 (4.55%) 1		
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all) Haemoglobinuria subjects affected / exposed occurrences (all) Chromaturia subjects affected / exposed occurrences (all) Bilirubinuria subjects affected / exposed occurrences (all)	 0 / 22 (0.00%) 0 0 / 22 (0.00%) 0 1 / 22 (4.55%) 2 0 / 22 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Arthritis subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Flank pain	 1 / 22 (4.55%) 1 0 / 22 (0.00%) 0 1 / 22 (4.55%) 1		

subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Muscle fatigue			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Enterovirus infection			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Gingivitis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Lyme disease			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	3		
Pharyngitis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Cystitis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		

Conjunctivitis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
COVID-19 subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Wound infection subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		
Vitamin B12 deficiency subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2018	- To allow randomization ≤ 8 days before the first dose of IP administration and add RBC transfusion received within the last 12 months as stratification factor. - To update text describing dosing schedule for participants who require dose adjustments for IP based on signs and symptoms of intravascular hemolysis, including LDH levels. - To update statistical sections - To clarify study discontinuation procedures for participants who develop meningococcal infection, who become pregnant, or who require continuous dose adjustments for IP. - To clarify urine collection for hemoglobinuria assessment. - To add dates for concomitant medications. - To remove outcome from blood transfusion data collected. - To clarify laboratory testing category for hemolysis-related laboratory tests. - To update site geographical regions. - To update inclusion/exclusion criteria. - To update sampling schedule for serum chemistry, hematology, hemolysis-related tests, and coagulation. - To add follow-up period information. - To reduce liver Doppler ultrasound assessments to screening only. - To add and clarify C-reactive protein sample collection.
29 April 2019	- To update the planned number of sites from 12 to 25 and to clarify that the study would be performed globally and not only in Europe. - To update the planned study duration from approximately 24 months to approximately 27 months. - To update the planned study start and end dates. - To remove subgroup analyses by age and ethnicity for the safety analysis set.
05 March 2020	- To update the number of planned study sites from 25 to 45. - To update the threshold of the aggregated intra-subject coefficient of variation (CV). - To update the primary endpoint for the crossover comparison to include an additional assessment period. - To add the End of Study definition as last participant, last visit. - To clarify text in the Prior and Concomitant Therapy section to include prophylactic antibiotics as concomitant medications. - To update the timing the first blinded interim check of CV. - To clarify the criteria for discontinuation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported