Clinical trial results:
An Open-Label Extension Study to Evaluate the Long-Term Safety, Tolerability, and Efficacy of REGN3918 in Patients with Paroxysmal Nocturnal Hemoglobinuria

Summary

EudraCT number	2019-000130-20
Trial protocol	NL CZ GB HU IT
Global end of trial date	07 April 2022

Results information

Result version number	v1 (current)
This version publication date	20 April 2023
First version publication date	20 April 2023

Trial information

Trial identification

Sponsor protocol code	R3918-PNH-1868

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04162470
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Road, Tarrytown, 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)	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	07 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 April 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 long-term safety, tolerability, and effect on intravascular hemolysis of REGN3918 in participants with paroxysmal nocturnal hemoglobinuria (PNH).

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	03 December 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Malaysia: 4
Country: Number of subjects enrolled	Taiwan: 4
Country: Number of subjects enrolled	United Kingdom: 2
Worldwide total number of subjects	24
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)	20
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the study, the sponsor made an administrative decision to terminate the pozelimab monotherapy program, all participants were withdrawn from this study.

Period 1

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

Arms

Arm title	REGN3918

Arm description:

Participants who completed parent study R3918-PNH-1852 (2018-002734-20) received pozelimab 800 milligrams (mg) subcutaneous (SC) injection once weekly (QW) for up to 104 weeks.

Arm type	Experimental
Investigational medicinal product name	Pozelimab
Investigational medicinal product code	REGN3918
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received pozelimab 800 mg SC injection QW for up to 104 weeks.

Number of subjects in period 1	REGN3918
Started	24
Completed	0
Not completed	24
Withdrawn due to sponsor’s decision	24

Baseline characteristics

Reporting groups	
Reporting group title	REGN3918
Reporting group description:	
Participants who completed parent study R3918-PNH-1852 (2018-002734-20) received pozelimab 800 milligrams (mg) subcutaneous (SC) injection once weekly (QW) for up to 104 weeks.	

Reporting group values	REGN3918	Total	
Number of subjects	24	24	
Age categorical Units: Participants			
Age continuous Units: years			
arithmetic mean	45.8		
standard deviation	± 17.26	-	
Gender categorical Units: Participants			
Female	11	11	
Male	13	13	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	21	21	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	2	2	
More than one race	0	0	
Unknown or Not Reported	1	1	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	24	24	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	REGN3918

Reporting group description:

Participants who completed parent study R3918-PNH-1852 (2018-002734-20) received pozelimab 800 milligrams (mg) subcutaneous (SC) injection once weekly (QW) for up to 104 weeks.

Primary: Number of Participants with Treatment-emergent Adverse Events (TEAEs) and Serious TEAEs

End point title	Number of Participants with Treatment-emergent Adverse Events (TEAEs) and Serious TEAEs[1]

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a subject or clinical investigation participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. TEAEs was defined as AEs that developed or worsened during the on-treatment period. SAE was defined as any untoward medical occurrence that resulted in any of following outcomes: death, life-threatening, required initial/prolonged in-participant hospitalization, persistent/significant disability/incapacity, congenital anomaly/birth defect/considered as medically important event. TEAEs included both Serious TEAEs and non-serious TEAEs. Safety Analysis Set (SAF) included all enrolled participants who received any study drug.

End point type	Primary

End point timeframe:

Baseline up to Week 104

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not applicable to this endpoint.

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Participants				
Participants with TEAEs	15			
Participants with Serious TEAEs	2			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants who Achieved Lactate Dehydrogenase (LDH) Less Than or Equal to (≤) 1.5* ULN From Baseline to Week 26

End point title	Percentage of Participants who Achieved Lactate Dehydrogenase (LDH) Less Than or Equal to (≤) 1.5* ULN From Baseline to Week 26[2]

End point description:

Percentage of participants who achieved LDH ≤1.5* Upper limit of normal (ULN) over Week 26, defined as LDH ≤1.5*ULN from baseline up to Week 26 were reported. A participant was considered to have met the criteria for adequate control of intravascular hemolysis if all of their LDH readings from the baseline through Week 26 inclusive or through the analysis end date, whichever is earlier, had values ≤ 1.5*ULN.

Full Analysis Set (FAS) included all enrolled participants who received any study drug. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline up to Week 26

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not applicable to this endpoint.

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Percentage of participants				
number (confidence interval 95%)	95.7 (87.3 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Rate of Transfusion with Red Blood Cells (RBCs) Through Week 26

End point title	Overall Rate of Transfusion with Red Blood Cells (RBCs) Through Week 26

End point description:

The overall rate of transfusion for a participant was calculated based on the duration of treatment exposure of the participant. FAS included all enrolled participant who received any study drug.

End point type	Secondary

End point timeframe:

Baseline up to Week 26

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Rate per person-year of treatment				
number (confidence interval 95%)	0.164 (0.006 to 4.678)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Had Breakthrough Hemolysis Through Week 26 and 78

End point title	Percentage of Participants who Had Breakthrough Hemolysis Through Week 26 and 78

End point description:

A participant was considered to have breakthrough hemolysis if he/she had any LDH measurement greater than or equal to (≥) 2*ULN, concomitant with associated signs or symptoms at any time subsequent to an initial achievement of disease control (i.e., LDH ≤ 1.5* ULN). FAS included all enrolled participants who received any study drug. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n= number analysed" signifies those participants who were evaluable at the specified timepoint.

End point type	Secondary

End point timeframe:

At Week 26 and 78

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Percentage of participants				
number (confidence interval 95%)				
At Week 26 (n=23)	0 (0 to 0)			
At Week 78 (n=15)	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved Adequate Control of Intravascular Hemolysis Through Week 78

End point title	Percentage of Participants who Achieved Adequate Control of Intravascular Hemolysis Through Week 78

End point description:

A participant was considered to have met the criteria for adequate control of intravascular hemolysis if all of his/her LDH readings from the baseline through Week 78 inclusive or through the analysis end date, whichever is earlier, had values ≤1.5* ULN. and must not have discontinued study treatment early. FAS included all enrolled participants who received any study drug. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline up to Week 78

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Percentage of participants				
number (confidence interval 95%)	93.8 (81.9 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who are Transfusion-free (with RBCs) Through Week 26 and 78

End point title	Percentage of Participants who are Transfusion-free (with RBCs) Through Week 26 and 78

End point description:

Transfusion free was defined as not having received an RBC transfusion during the first 26 and 78 weeks. A transfusion was counted only if it was per-protocol, that is, if it follows the predefined transfusion algorithm: RBC transfusion due to a post-baseline hemoglobin level less than (<) 9 gram per deciliter (g/dL) (with anemia symptoms) or a post-baseline hemoglobin level < 7 g/dL (without anemia symptoms). FAS included all enrolled participants who received any study drug. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n= number analysed" signifies those participants who were evaluable at the specified timepoint.

End point type	Secondary

End point timeframe:

At Week 26 and 78

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Percentage of participants				
number (confidence interval 95%)				
At Week 26 (n=23)	95.7 (87.3 to 100.0)			
At Week 78 (n=16)	93.8 (81.9 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Achieved Normalization of Intravascular Hemolysis Through Week 26 and Week 78

End point title	Percentage of Participants who Achieved Normalization of Intravascular Hemolysis Through Week 26 and Week 78

End point description:

A participant was considered to have met the criteria for adequate control of intravascular hemolysis if all of his/her LDH readings from the baseline through Week 78 inclusive or through the analysis end date, whichever is earlier, had values ≤1.5* ULN. and must not have discontinued study treatment early. FAS included all enrolled participants who received any study drug. Here, "n= number analysed" signifies those participants who were evaluable at the specified timepoint.

End point type	Secondary
End point timeframe:	
At Week 26 and 78	

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of participants				
number (confidence interval 95%)				
At Week 26 (n=24)	75.0 (57.7 to 92.3)			
At Week 78 (n=20)	55.0 (33.2 to 76.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in LDH Levels at Week 26, 78, and 104

End point title	Percent Change From Baseline in LDH Levels at Week 26, 78, and 104
End point description:	
Percent change from baseline in LDH levels at Week 26, 78, and 104 was reported. Reported baseline is from R3918-PNH-1852 study. FAS included all enrolled participants who received any study drug. Here, "n= number analysed" signifies those participants who were evaluable at the specified timepoint.	
End point type	Secondary
End point timeframe:	
Baseline, Week 26, 78, and 104	

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percent change				
arithmetic mean (standard deviation)				
At Week (n=24)	-81.900 (± 8.9226)			
At Week 78 (n=17)	-84.256 (± 8.1412)			
At Week 104 (n=15)	-83.930 (± 7.6705)			

Statistical analyses

No statistical analyses for this end point

Secondary: Changes From Baseline in LDH Levels at Week 26, 78, and 104

End point title	Changes From Baseline in LDH Levels at Week 26, 78, and 104

End point description:

Change from baseline in LDH levels at Week 26, 78, and 104 was reported. Reported baseline is from R3918-PNH-1852 study. FAS included all enrolled participants who received any study drug. Here, "n= number analysed" signifies those participants who were evaluable at the specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26, 78, and 104

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Units per liter (U/L)				
arithmetic mean (standard deviation)				
At Week 26 (n=24)	-5.098 (± 2.5695)			
At Week 78 (n=17)	-5.395 (± 2.8468)			
At Week 104 (n=15)	-5.270 (± 2.9057)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Red Blood Cell (RBC) Hemoglobin Levels at Week 26, 78, and 104

End point title	Change From Baseline in Red Blood Cell (RBC) Hemoglobin Levels at Week 26, 78, and 104

End point description:

Change from baseline in RBC hemoglobin levels at Week 26, 78, and 104 was reported. FAS included all enrolled participants who received any study drug. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n= number analysed" signifies those participants who were evaluable at the specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26, 78, and 104

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Gram per liter (g/l)				
arithmetic mean (standard deviation)				
At Week 26 (n=21)	3.6 (± 8.97)			
At Week 78 (n=14)	5.3 (± 17.20)			
At Week 104 (n=5)	-2.4 (± 16.56)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Free Hemoglobin Levels at Week 26, 78 and 104

End point title	Change From Baseline in Free Hemoglobin Levels at Week 26, 78 and 104

End point description:

Change from baseline in free hemoglobin levels at Week 26, 78 and 104 was reported. FAS included all enrolled participants who received any study drug. Here, "number of participants analysed" signifies participants who were evaluable for this endpoint and "n= number analysed" signifies those participants who were evaluable at the specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26, 78 and 104

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Milligram per deciliter (mg/dL)				
arithmetic mean (standard deviation)				
At Week 26 (n=16)	-1.39 (± 6.929)			
At Week 78 (n=7)	-0.56 (± 2.196)			
At Week 104 (n=4)	-0.93 (± 1.153)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Total REGN3918

End point title	Serum Concentrations of Total REGN3918

End point description:

Serum Concentrations of total REGN3918 was reported.

End point type	Secondary

End point timeframe:

Pre-dose (Day 1), End of infusion at Week 13, 26, 39, 52, 65, 78, 91 and 104

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: Milligrams per Liter (mg/L)				
arithmetic mean (standard deviation)				
Pre-dose (Day 1) (n=23)	423 (± 218)			
Week 13 (n=23)	398 (± 203)			
Week 26 (n=23)	401 (± 212)			
Week 39 (n=18)	420 (± 216)			
Week 52 (n = 17)	413 (± 202)			
Week 65 (n = 16)	438 (± 207)			
Week 78 (n = 10)	433 (± 266)			
Week 91 (n = 8)	483 (± 278)			
Week 104 (n = 0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-Emergent Anti-Drug Antibodies (ADA) to REGN3918

End point title	Number of Participants with Treatment-Emergent Anti-Drug Antibodies (ADA) to REGN3918

End point description:

Number of participants with treatment-emergent ADA response to REGN3918 was reported.

Here, "number analyzed" signifies those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline up to Week 104

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Participants				
Treatment-Emergent ADA	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose to Week 104	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	Pozelimab

Reporting group description:

Participants who completed parent study R3918-PNH-1852 (2018-002734-20) received pozelimab 800 milligrams (mg) subcutaneous (SC) injection once weekly (QW) for up to 104 weeks.

Serious adverse events	Pozelimab		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 24 (8.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pozelimab		
Total subjects affected by non-serious adverse events subjects affected / exposed	6 / 24 (25.00%)		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
General disorders and administration site conditions Chills subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Gastrointestinal disorders Mouth ulceration subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported