EU Clinical Trials Register

Clinical trial results:

An Open Label, Single Arm Study to Evaluate the Efficacy and Safety of REGN3918 in Patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) Who Are Complement Inhibitor Naive or Have Not Recently Received Complement Inhibitor Therapy

Summary

EudraCT number	2018-002734-20
Trial protocol	CZ GB HU NL IT
Global end of trial date	10 June 2021

Results information

Result version number	v1 (current)
This version publication date	24 June 2022
First version publication date	24 June 2022

Trial information

Trial identification

Sponsor protocol code	R3918-PNH-1852

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03946748
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Rd., 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	10 June 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 June 2021
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 demonstrate a reduction in intravascular hemolysis by REGN3918 over 26 weeks of treatment in subjects with active PNH who are treatment naive to complement inhibitor therapy or have not recently received complement inhibitor therapy.

Protection of trial subjects:

It was the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study was 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	16 May 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	United Kingdom: 2
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Malaysia: 4
Country: Number of subjects enrolled	Taiwan: 4
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:

Sponsor made administrative decision to stop enrollment to pursue combination program of REGN3918 & cemdisiran for treatment of Paroxysmal Nocturnal Hemoglobinuria (PNH). Study not stopped due to safety concerns or lack of efficacy. 28 screened, 24 were enrolled & treated: 4 screen failures (1-Lost to follow-up, 1-did not meet criteria, 1-other).

Period 1

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

Arms

Arm title	REGN3918

Arm description:

Participants received a single loading dose of REGN3918 30 milligrams per kilogram (mg/kg) intravenous (IV) infusion on Day 1, followed by a maintenance regimen of 800 milligrams (mg) subcutaneous (SC) injection on Day 8 once weekly (QW) up to 26 weeks of treatment period.

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

Dosage and administration details:

Participants received REGN3918 30 mg/kg IV infusion, followed by a maintenance regimen of 800 mg SC injection up to 26 weeks of treatment period.

Number of subjects in period 1	REGN3918
Started	24
Completed	24

Baseline characteristics

Reporting groups

Reporting group title	Overall study

Reporting group description:

Participants received a single loading dose of REGN3918 30 milligrams per kilogram (mg/kg) intravenous (IV) infusion on Day 1, followed by a maintenance regimen of 800 milligrams (mg) subcutaneous (SC) injection on Day 8 once weekly (QW) up to 26 weeks of treatment period.

Reporting group values	Overall study	Total	
Number of subjects	24	24	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	45.4		
standard deviation	± 17.28	-	
Gender categorical			
Units: Subjects			
Female	11	11	
Male	13	13	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	24	24	
Unknown or Not Reported	0	0	
Race (NIH/OMB)			
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	

End points

End points reporting groups

Reporting group title	REGN3918

Reporting group description:

Participants received a single loading dose of REGN3918 30 milligrams per kilogram (mg/kg) intravenous (IV) infusion on Day 1, followed by a maintenance regimen of 800 milligrams (mg) subcutaneous (SC) injection on Day 8 once weekly (QW) up to 26 weeks of treatment period.

Primary: Percentage of Participants Who Achieved Adequate Control of Intravascular Hemolysis

End point title	Percentage of Participants Who Achieved Adequate Control of Intravascular Hemolysis[1]

End point description:

Participants were considered to have had adequate control of intravascular hemolysis if all of their lactose dehydrogenase (LDH) readings from Week 4 through Week 26 inclusive had values less than or equal to ≤ 1.5 × upper limit of normal (ULN). Participants must have more than equal to (≥) 50 percent (%) of scheduled LDH measures in those weeks, must not have had more than (>) 2 consecutive visits without LDH measures, must not have experienced breakthrough hemolysis, and must not have discontinued study treatment early. Participants were considered not to have had adequate control of intravascular hemolysis if they failed any of these criteria. Full analysis set (FAS) included all enrolled participants who received any study drug.

End point type	Primary

End point timeframe:

Week 4 through Week 26

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: Results were descriptively summarized.

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of Participants				
number (confidence interval 95%)	75.0 (57.7 to 92.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Achieved Transfusion Avoidance

End point title	Percentage of Participants Who Achieved Transfusion

End point description:

Transfusion avoidance was defined as not having received red blood cell (RBC) transfusion during the first 26 weeks. A transfusion was counted only if it is per-protocol, that is, it follows the predefined transfusion algorithm: RBC transfusion due to a post-baseline hemoglobin level < 9 grams per deciliter (g/dL) (with anemia symptoms) or a post-baseline hemoglobin level < 7 g/dL (without anemia symptoms). The FAS included all enrolled participants who received any study drug.

End point type	Primary

End point timeframe:

Up to 26 Weeks

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: Results were descriptively summarized.

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of Participants				
number (confidence interval 95%)	87.5 (74.3 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Had Breakthrough Hemolysis (BTH)

End point title	Percentage of Participants Who Had Breakthrough Hemolysis (BTH)
End point description:	

Breakthrough hemolysis was defined as the measurement of LDH ≥ 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). The FAS included all enrolled subjects who received any study drug.

End point type	Secondary
End point timeframe:	

Baseline up to 26 Weeks

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieved Normalization of Intravascular Hemolysis

End point title	Percentage of Participants Who Achieved Normalization of Intravascular Hemolysis
End point description:	

A participant was considered to have achieved normalization of intravascular hemolysis if their LDH readings between Week 4 through Week 26 inclusive had values ≤ 1.0 ULN. A participant must have ≥

50% of scheduled LDH measures in those weeks, must not have had > 2 consecutive visits without LDH measures, must not have experienced breakthrough hemolysis, and must not have discontinued study treatment early. A participant was considered not to have achieved normalization of intravascular hemolysis if they failed any of these criteria. The FAS included all enrolled participants who received any study drug.

End point type	Secondary

End point timeframe:
Week 4 through Week 26

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of Participants				
number (confidence interval 95%)	16.7 (1.8 to 31.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Lactate Dehydrogenase (LDH) ≤ 1.5 x ULN

End point title	Time to First Lactate Dehydrogenase (LDH) ≤ 1.5 x ULN

End point description:

A time-to-first-event analysis was used to estimate the proportion of participants achieving transfusion avoidance at week 26 and a 95% confidence interval. As per changes in planned analysis, the sponsor made an administrative decision to close enrollment for this study due to a change in the clinical development program. Hence, this endpoint was not analyzed.

End point type	Secondary

End point timeframe:
Up to Week 26

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Weeks				
median (full range (min-max))	(to)			

Notes:

[3] - Sponsor made administrative decision to close enrollment. Hence, this endpoint was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Days With LDH ≤ 1.5 ULN From Week 4 Through Week 26

End point title	Percentage of Days With LDH ≤ 1.5 ULN From Week 4 Through

	Week 26

End point description:

Percentage of days was calculated as number of days with LDH ≤ 1.5 x ULN divided by the participants' total treatment duration (total number of days on treatment from Week 4 through Week 26). LDH ≤ 1.5 x ULN was used as an indicator of adequate control of intravascular hemolysis. The FAS included all enrolled participants who received any study drug.

End point type	Secondary

End point timeframe:

Week 4 through Week 26

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percentage of Days				
arithmetic mean (standard deviation)	93.4 (± 18.76)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in LDH Levels at Week 26

End point title	Change From Baseline in LDH Levels at Week 26

End point description:

Change from baseline in LDH levels at Week 26 was reported. The FAS included all enrolled participants who received any study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Units per liter (U/L)				
least squares mean (standard error)	-5.070 (± 0.1467)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in LDH Levels at Week 26

End point title	Percent Change From Baseline in LDH Levels at Week 26

End point description:

Percent change from baseline in LDH levels at Week 26 was reported. The FAS included all enrolled participants who received any study drug.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Percent Change				
least squares mean (standard error)	-81.72 (± 1.847)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Transfusion With Red Blood Cells (RBCs)

End point title	Rate of Transfusion With Red Blood Cells (RBCs)

End point description:

The rate of transfusion with RBCs for a participant was the total number of transfusions divided by total person-years of time on treatment. The FAS included all enrolled participants 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: Infusions Per Participant Year				
number (confidence interval 95%)	1.039 (0.187 to 5.772)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Units of Transfusion With RBCs

End point title	Number of Units of Transfusion With RBCs

End point description:

Transfusions with RBCs proceeded according to the following predefined criteria that triggered a transfusion; however, the actual number of units to be transfused is at the discretion of the investigator: • Transfuse with RBC(s) if the post-baseline hemoglobin level is <9 g/dL with symptoms resulting from anemia or • Transfuse with RBC(s) if the post-baseline hemoglobin level is <7 g/dL. As per changes in planned analysis, the sponsor made an administrative decision to close enrollment for this study due to a change in the clinical development program. Hence, this endpoint was not analyzed.

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	0[4]			
Units: Number of Units				
number (not applicable)				

Notes:

[4] - Sponsor made administrative decision to close enrollment. Hence, this endpoint was not analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Free Hemoglobin Levels at Week 26

End point title	Change From Baseline in Free Hemoglobin Levels at Week 26

End point description:

Change from baseline in free hemoglobin levels at Week 26 was assessed. The safety analysis set (SAF) included all enrolled participants who received any study drug. Here, "number of subjects analysed" signifies those participants who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: milligrams per Deciliter (mg/dL)				
arithmetic mean (standard deviation)	-9.19 (± 16.264)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in RBC Hemoglobin Levels at Week 26

End point title	Change From Baseline in RBC Hemoglobin Levels at Week 26
End point description:	
Hemoglobin levels in participants with PNH was measured. Change from baseline in RBC hemoglobin at Week 26 was reported. The FAS included all enrolled participants who received any study drug.	
End point type	Secondary
End point timeframe:	
Baseline, Week 26	

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: grams per Liter (g/L)				
least squares mean (standard error)	15.0 (± 3.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Complement Hemolytic Activity Assay (CH50) at Week 26

End point title	Change From Baseline in Total Complement Hemolytic Activity Assay (CH50) at Week 26
End point description:	
Change from baseline in total CH50 at Week 26 was reported. Here "International units per milliliter" was abbreviated as "IU/mL". The FAS included all enrolled participants who received any study drug. Here, "number of subjects analysed" signifies those participants who were evaluable for this endpoint.	
End point type	Secondary
End point timeframe:	
Baseline, Week 26	

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: IU/mL				
least squares mean (standard error)	-236.6 (± 0.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in CH50 up to Week 26

End point title	Percent Change From Baseline in CH50 up to Week 26
End point description:	
Percent change from baseline in CH50 up to Week 26 was reported. The FAS included all enrolled participants who received any study drug. Here, "number of subjects analysed" signifies those participants who were evaluable for this endpoint.	
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	23			
Units: Percent Change				
least squares mean (standard error)				
Percent Change From Baseline in CH50	-99.99 (± 0.243)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) at Week 26

End point title	Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) at Week 26
End point description:	
The FACIT-F was a 13-item, self-reported PRO measure assessing an individual's level of fatigue during their usual daily activities over the past week. This questionnaire was part of the FACIT measurement system, a compilation of questions measuring health-related QoL in participants with cancer and other chronic illnesses. The FACIT-fatigue assessed the level of fatigue using a 4-point Likert scale ranging from 0 (not at all), 1 (a little bit), 2 (somewhat), 3 (quite a bit), 4 (very much) The sum of all responses resulted in the FACIT-F score for a total possible score of 0 to 52, with higher scores indicated greater fatigue. FAS population. Here, "number of subjects analyzed" signifies those participants who were evaluable for this endpoint.	
End point type	Secondary
End point timeframe:	
Baseline, Week 26	

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Score on a Scale				
least squares mean (standard error)	9.9 (± 1.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-core 30 (EORTC QLQ-C30) at Week 26

End point title	Change From Baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-core 30 (EORTC QLQ-C30) at Week 26

End point description:

EORTC QLQ-C30 was a 30-item questionnaire used to assess symptoms & side effects of treatment. It consists of 15 domains: 5 multi-item functioning scales (physical, role, social, emotional & cognitive), answered on 4-point scale (1=Not at all,2=A Little,3=Quite a Bit,4=Very Much). Each score ranges: 0-100; higher score indicates higher level of functioning & better QoL. A global health status/QoL scale answered on 7-point scale (1=Very Poor to 7=Excellent). Each score ranges: 0-100; higher score indicates better QoL. 9 symptom scales (Fatigue, Nausea/Vomiting, Pain, Dyspnea, Insomnia, Appetite Loss, Constipation, Diarrhea, Financial Impact), answered on 4-point scale (1=Not at all, 2=A Little, 3=Quite a Bit, 4=Very Much). Each score ranges:0-100; higher score indicates higher level of symptoms, & negative change from baseline indicates an improvement in symptoms. FAS population. Here, "number of subjects analysed" signifies those participants who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Score on a Scale				
least squares mean (standard error)				
Global Health status/quality: Change at Week 26	12.509 (± 3.2286)			
Physical Functioning: Change at Week 26	17.511 (± 2.6767)			
Cognitive Functioning: Change at Week 26	9.840 (± 2.9710)			
Social Functioning: Change at Week 26	15.846 (± 3.8036)			
Fatigue: Change at Week 26	-18.904 (± 2.9899)			
Pain: Change at Week 26	-13.537 (± 3.0315)			
Dyspnea: Change at Week 26	-15.874 (± 4.7953)			
Emotional Functioning: Change at Week 26	14.457 (± 3.8645)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Quality of Life-5 Dimensions-3 Level (EQ-5D-3L) Index Score at Week 26

End point title	Change From Baseline in European Quality of Life-5 Dimensions-3 Level (EQ-5D-3L) Index Score at Week 26

End point description:

EQ-5D-3L was a self-administered standardized instrument for use as measure of health outcome. It comprised 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension rated on 3 levels scale: 1 (no problems), 2 (some problems), 3 (extreme problems). The summed score ranges from 5-15 with "5" corresponding to no problems and "15" to severe problems in 5 dimensions. EQ-5D index calculated by applying preference-based weights (tariffs) to scores of five health state dimensions. Index values range from -1 to 1, with 0 representing a health state equivalent to death and 1 representing perfect health. Total index EQ-5D-3L summary score was weighted with a range of -0.594 (worst) to 1.0 (best). FAS included all enrolled participants who received any study drug. Here, "number of subjects analysed" signifies those participants who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Score on a Scale				
least squares mean (standard error)	0.136 (± 0.0238)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EQ-5D-3L Visual Analogue Scale (VAS) at Week 26

End point title	Change From Baseline in EQ-5D-3L Visual Analogue Scale (VAS) at Week 26

End point description:

The EQ-5D-3L was a standardized instrument for use as a measure of health outcome and was administered to all subjects to assess the effect of the treatment on the participants' quality of life. The EQ-5D-3L includes a visual analog scale (VAS) which is a vertical scale with numbers ranging from 0 to 100. Participants were asked to draw a line to the place on the scale that best represented how good or bad his health was on that day. The worst state a participant can imagine was marked zero, and the best state the participant can imagine was marked 100. Mean change in VAS score from baseline was

reported. The FAS included all enrolled participants who received any study drug. Here, "number of subjects analysed" signifies those participants who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Score on a Scale				
least squares mean (standard error)	8.4 (± 2.18)			

Statistical analyses

No statistical analyses for this end point

Secondary: 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

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant 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. The SAF included all enrolled participants 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: Participants				
Participants with TEAEs	21			
Participants with Serious TEAEs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs Based on Severity

End point title	Number of Participants With TEAEs Based on Severity

End point description:

An AE was defined as any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. Severity of AEs was graded according to the following scale, Mild: event that does not generally interfere with usual activities of daily living; Moderate: event that interferes with usual activities of daily living, causing discomfort, permanent risk of harm; Severe: AE that interrupts usual activities of daily living, significantly affects clinical status, or may require intensive therapeutic intervention. The SAF included all enrolled participants who received any study drug. Here, "number of subjects analysed" signifies those participants who were evaluable for this endpoint.

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	21			
Units: Participants				
Participants with Mild TEAEs	13			
Participants with Moderate TEAEs	6			
Participants with Severe TEAEs	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Meaningful Changes in Clinical Laboratory Parameters

End point title	Number of Participants With Clinically Meaningful Changes in Clinical Laboratory Parameters

End point description:

Clinical laboratory parameters included biochemistry, hematology and urinalysis. Number of participants with potential clinically significant changes in laboratory parameters which were deemed clinically significant by the investigator were reported. The SAF included all enrolled participants 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: Participants				
Hematology	13			
Chemistry	17			
Urinalysis	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Meaningful Changes in Vital Signs

End point title	Number of Participants With Clinically Meaningful Changes in Vital Signs

End point description:

Vital sign assessments included pulse rate, blood pressure (systolic and diastolic blood pressure) and body temperature. Number of participants with potential clinically meaningful changes in vital signs which were deemed clinically significant by the investigator were reported. The SAF included all enrolled participants 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: Participants	12			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Meaningful Changes in 12-lead Electrocardiograms (ECGs)

End point title	Number of Participants With Clinically Meaningful Changes in 12-lead Electrocardiograms (ECGs)

End point description:

12-lead ECGs were evaluated. Any change in ECG assessments which are deemed clinically significant by the investigator were reported. The FAS included all enrolled participants 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: Participants	0			

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. The pharmacokinetic (PK) analysis set includes all participants who received any study drug and who had at least 1 non-missing result for concentration of REGN3918 following the first dose of study drug. Participants will be analyzed according to the treatment actually received. Here, "n= number analysed" signifies those participants who were evaluable at the specified categories.

End point type	Secondary

End point timeframe:

Pre-dose (Day 0), End of infusion at Days 0, 2, 7, 28, 56, 84, 112, 140, and 182

End point values	REGN3918			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: milligram/Liter (mg/L)				
arithmetic mean (standard deviation)				
At Day 0 (Pre-dose) (n=24)	0 (± 0)			
At Day 0 (End of Infusion) (n=24)	605 (± 214)			
At Day 2 (End of Infusion) (n-24)	429 (± 159)			
At Day 7 (End of Infusion) (n=24)	292 (± 80.5)			
At Day 28 (End of Infusion) (n=23)	324 (± 97.5)			
At Day 56 (End of Infusion) (n=22)	368 (± 148)			
At Day 84 (End of Infusion) (n=22)	363 (± 152)			
At Day 112 (End of Infusion) (n=23)	379 (± 186)			
At Day 140 (End of Infusion) (n=23)	430 (± 225)			
At Day 182 (End of infusion) (n=24)	435 (± 221)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-emergent Anti-Drug Antibodies (ADA) Response to REGN3918

End point title	Number of Participants With Treatment-emergent Anti-Drug Antibodies (ADA) Response to REGN3918

End point description:

Number of participants with treatment-emergent ADA response to REGN3918 was reported. The ADA analysis set (AAS) included all participants who received any study drug and who had at least 1 non-missing ADA result from the REGN3918 ADA assay after the first dose of 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: Participants	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 26	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	REGN3918
Reporting group description:	
Participants received a single loading dose of REGN3918 30 milligrams per kilogram (mg/kg) intravenous (IV) infusion on Day 1, followed by a maintenance regimen of 800 milligrams (mg) subcutaneous (SC) injection on Day 8 once weekly (QW) up to 26 weeks of treatment period.	

Serious adverse events	REGN3918		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	REGN3918		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 24 (54.17%)		
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 24 (37.50%)		
occurrences (all)	10		
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	7		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 June 2019	Protocol Amendment 2: Removed Sponsor as a responsible party in the confirmation of a breakthrough hemolysis event. Added language to clarify that blood collection should occur if a breakthrough hemolysis event is suspected. Updated the duration of the open-label extension study. Removed irrelevant information related to blinding for the interim analysis. This is an open-label study. Revised exclusion requirement for peripheral blood absolute neutrophil count to <500/µL. Revised description of PNH erythrocytes and granulocytes to reflect typical laboratory output for these analytes. Updated inclusion criterion #3 to specify PNH granulocytes that are denoted as polymorphonuclear (PMN).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported