



## Clinical trial results:

### A Phase 2a, Open-Label, Multiple Dose Study to Assess the Safety, Efficacy, and Pharmacokinetics of Subcutaneously Administered APL-2 in Subjects with Paroxysmal Nocturnal Hemoglobinuria (PNH)

#### Summary

EudraCT number	2017-005140-16
Trial protocol	BG GR
Global end of trial date	22 October 2019

#### Results information

Result version number	v1 (current)
This version publication date	22 October 2020
First version publication date	22 October 2020

#### Trial information

##### Trial identification

Sponsor protocol code	APL2-202
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03593200
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	Apellis Pharmaceuticals, Inc
Sponsor organisation address	100 5th Avenue, Waltham, Massachusetts, United States, 02451
Public contact	Apellis Clinical Trial Information Line, Apellis Pharmaceuticals, Inc, 1 833-284-6361, clinicaltrials@apellis.com
Scientific contact	Apellis Clinical Trial Information Line, Apellis Pharmaceuticals, Inc, 1 833-284-6361, clinicaltrials@apellis.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	22 October 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	22 October 2019
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To assess safety, tolerability, preliminary efficacy, and pharmacokinetics (PK) of multiple subcutaneous (SC) doses of pegcetacoplan in subjects with paroxysmal nocturnal hemoglobinuria (PNH) who had not received treatment with eculizumab (Soliris®) in the past. The proposed dosage of pegcetacoplan was 270 milligrams (mg)/day.

Protection of trial subjects:

This research was carried out in accordance with the protocol, applicable regulations, the ethical principles set forth in the Declaration of Helsinki, and the International Council for Harmonisation Good Clinical Practice E6 (R2) guideline.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 August 2018
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	Bulgaria: 2
Country: Number of subjects enrolled	Serbia: 2
Worldwide total number of subjects	4
EEA total number of subjects	2

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)	4
From 65 to 84 years	0



## Subject disposition

### Recruitment

Recruitment details:

This Phase 2a, open-label, multiple-dose study was conducted in subjects with PNH who had not received treatment with eculizumab (Soliris®) in the past, between 16 August 2018 and 22 October 2019.

### Pre-assignment

Screening details:

Up to 20 subjects were planned to be enrolled; however, the sponsor decided to close recruitment after 4 subjects were enrolled based on the conclusion that sufficient data were collected to meet the study objectives.

### Period 1

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

### Arms

<b>Arm title</b>	Pegcetacoplan 270 mg/day
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Arm description:

Subjects received SC infusions of pegcetacoplan 270 mg/day up to Day 364. Intrasubject dose escalation up to a dosage of 360 mg/day was permitted if clinically indicated.

Arm type	Experimental
Investigational medicinal product name	Pegcetacoplan
Investigational medicinal product code	
Other name	APL-2
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Pegcetacoplan was administered as a sterile solution up to 40 mg/milliliter (mL) in acetate-buffered mannitol administered by SC infusion. Subjects self-administered the SC infusions after receiving appropriate training by a research nurse or other study personnel.

<b>Number of subjects in period 1</b>	Pegcetacoplan 270 mg/day
Started	4
Completed	4

## Baseline characteristics

### Reporting groups

Reporting group title	Pegcetacoplan 270 mg/day
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Reporting group description:

Subjects received SC infusions of pegcetacoplan 270 mg/day up to Day 364. Intrasubject dose escalation up to a dosage of 360 mg/day was permitted if clinically indicated.

Reporting group values	Pegcetacoplan 270 mg/day	Total	
Number of subjects	4	4	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	30.8 ± 11.81	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	1	1	
Race Units: Subjects			
White	4	4	
Ethnicity Units: Subjects			
Not Hispanic or Latino	4	4	

## End points

### End points reporting groups

Reporting group title	Pegcetacoplan 270 mg/day
Reporting group description: Subjects received SC infusions of pegcetacoplan 270 mg/day up to Day 364. Intrasubject dose escalation up to a dosage of 360 mg/day was permitted if clinically indicated.	

### Primary: Number of subjects with Treatment Emergent Adverse Events (TEAEs) Including by Severity

End point title	Number of subjects with Treatment Emergent Adverse Events (TEAEs) Including by Severity <sup>[1]</sup>
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#### End point description:

TEAEs were defined as adverse events (AE) that occurred after dosing on Day 1 and up to 30 days after the last dose of study drug. A treatment-related TEAE was defined as a TEAE with a relationship to study drug of possible, probable, or definite. TEAEs were graded according to the Common Terminology Criteria for Adverse Events (v4.03) based on: Grade 1: Mild, Grade 2: Moderate, Grade 3: Severe, Grade 4: Life-threatening, Grade 5: Death related to AE. Analysis performed on the safety set consisting of all subjects who received at least 1 dose of study drug.

End point type	Primary
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#### End point timeframe:

From Day 1 to 30 days after the last dose (approximately 56 weeks)

#### 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: Only descriptive statistics were reported for this primary endpoint.

End point values	Pegcetacoplan 270 mg/day			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Participants				
All TEAEs	3			
Treatment-related TEAEs	2			
Serious TEAEs	1			
TEAEs leading to study drug discontinuation	0			
TEAEs with mild intensity	2			
TEAEs with moderate intensity	0			
TEAEs with severe intensity	1			
TEAEs with life threatening intensity	0			
TEAEs leading to death	0			

### Statistical analyses

No statistical analyses for this end point

### Primary: Mean Change from Baseline in Lactate Dehydrogenase (LDH) Level

End point title	Mean Change from Baseline in Lactate Dehydrogenase (LDH)
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End point description:

Serum chemistry assessments of LDH were made at the last measurement prior to the first dose of pegcetacoplan (baseline) and periodically throughout the treatment period. Analysis performed on the Intent-to-treat (ITT) set consisting of all subjects who received at least 1 dose of study drug.

End point type Primary

End point timeframe:

Baseline and Day 365

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: Only descriptive statistics were reported for this primary endpoint.

<b>End point values</b>	Pegcetacoplan 270 mg/day			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: units/liter				
arithmetic mean (standard deviation)	-2322.8 ( $\pm$ 635.41)			

## Statistical analyses

No statistical analyses for this end point

### Primary: Mean Change from Baseline in Haptoglobin Level

End point title Mean Change from Baseline in Haptoglobin Level<sup>[3]</sup>

End point description:

Serum chemistry assessments of haptoglobin were made at the last measurement prior to the first dose of pegcetacoplan (baseline) and periodically throughout the treatment period. Analysis performed on the ITT set consisting of all subjects who received at least 1 dose of study drug.

End point type Primary

End point timeframe:

Baseline and Day 365

Notes:

[3] - 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: Only descriptive statistics were reported for this primary endpoint.

<b>End point values</b>	Pegcetacoplan 270 mg/day			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: grams/liter				
arithmetic mean (standard deviation)	0.08 ( $\pm$ 0.150)			

## Statistical analyses

No statistical analyses for this end point

## Primary: Mean Change from Baseline in Hemoglobin (Hb) Level

End point title	Mean Change from Baseline in Hemoglobin (Hb) Level <sup>[4]</sup>
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End point description:

Hematology assessments of Hb were made at the last measurement prior to the first dose of pegcetacoplan (baseline) and periodically throughout the treatment period. Analysis performed on the ITT set consisting of all subjects who received at least 1 dose of study drug.

End point type	Primary
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End point timeframe:

Baseline and Day 365

Notes:

[4] - 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: Only descriptive statistics were reported for this primary endpoint.

<b>End point values</b>	Pegcetacoplan 270 mg/day			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: grams/deciliter				
arithmetic mean (standard deviation)	5.27 (± 1.875)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change from Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Score

End point title	Mean Change from Baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Score
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End point description:

The FACIT-Fatigue scale is a 13 item Likert scaled instrument where the subject was presented with 13 statements and asked to indicate their response as it applied to the past 7 days. The 5 possible responses were 'Not at all' (0), 'A little bit' (1), 'Somewhat' (2), 'Quite a bit' (3) and 'Very much' (4). With 13 statements the total score had a range of 0 to 52. Higher score corresponds to a higher quality of life (QoL). Analysis performed on the ITT set consisting of all subjects who received at least 1 dose of study drug.

End point type	Secondary
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End point timeframe:

Baseline and Day 365

<b>End point values</b>	Pegcetacoplan 270 mg/day			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: score on a scale				
arithmetic mean (standard deviation)	6.5 (± 5.45)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change from Baseline in Absolute Reticulocyte Count (ARC) Level

End point title	Mean Change from Baseline in Absolute Reticulocyte Count (ARC) Level
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End point description:

Hematology assessments of ARC were made at the last measurement prior to the first dose of pegcetacoplan (baseline) and periodically throughout the treatment period. Analysis performed on the ITT set consisting of all subjects who received at least 1 dose of study drug.

End point type	Secondary
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End point timeframe:

Baseline and Day 365

<b>End point values</b>	Pegcetacoplan 270 mg/day			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ARC/nanoliter				
arithmetic mean (standard deviation)	-144.3 ( $\pm$ 98.51)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change from Baseline in Total Bilirubin Level

End point title	Mean Change from Baseline in Total Bilirubin Level
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End point description:

Serum chemistry assessments of total bilirubin were made at the last measurement prior to the first dose of pegcetacoplan (baseline) and periodically throughout the treatment period. Analysis performed on the ITT set consisting of all subjects who received at least 1 dose of study drug.

End point type	Secondary
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End point timeframe:

Baseline and Day 365

<b>End point values</b>	Pegcetacoplan 270 mg/day			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: micromoles/liter				
arithmetic mean (standard deviation)	-21.53 ( $\pm$ 8.358)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Number of Red Blood Cell (RBC) Transfusions per Month

End point title	Mean Number of Red Blood Cell (RBC) Transfusions per Month
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End point description:

The number of on-study RBC transfusions was monitored throughout the treatment period. Analysis performed on the ITT set consisting of all subjects who received at least 1 dose of study drug.

End point type	Secondary
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End point timeframe:

From Day 1 to Day 364

<b>End point values</b>	Pegcetacoplan 270 mg/day			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: transfusions				
arithmetic mean (full range (min-max))	0 (0 to 0)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change From Baseline in Linear Analog Scale Assessment (LASA) Score for QoL

End point title	Mean Change From Baseline in Linear Analog Scale Assessment (LASA) Score for QoL
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End point description:

The LASA consists of 3 items, where the respondents were asked to rate their perceived level of functioning. Specific domains included activity level, ability to carry out daily activities, and an item for overall QoL. Their level of functioning was reported on a 0 to 100 scale with 0 indicates "As low as could be" and 100 indicates "As high as could be". The combined score ranged from 0 to 300, with higher scores corresponding to a higher QoL. Analysis performed on the ITT set consisting of all subjects who received at least 1 dose of study drug.

Note: 9999999 indicates that a value was not calculated. Although data were collected for this endpoint, due to the small sample size, the individual values were listed and used for graphical presentation per subject over time only and therefore no summary statistics were prepared. Full range LASA change from baseline scores: 0 to 121.

End point type	Secondary
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End point timeframe:

Baseline and Day 365

<b>End point values</b>	Pegcetacoplan 270 mg/day			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: score on a scale				
arithmetic mean (standard deviation)	9999999 (± 9999999)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Serum Concentrations of Pegcetacoplan

End point title	Mean Serum Concentrations of Pegcetacoplan
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End point description:

Serum concentrations of pegcetacoplan at Day 365 are presented. Analysis performed on the PK set consisting of all subjects in the safety set who had at least 1 quantifiable PK sample post dose PK measurement.

Note: 9999999 indicates that a value was not calculated. Although data were collected for this endpoint, due to the small sample size, the individual values were listed and used for graphical presentation per subject over time only and therefore no summary statistics were prepared. Full range serum concentrations of pegcetacoplan: 512 to 703 microgram per milliliter (µg/mL).

End point type	Secondary
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End point timeframe:

Day 365

<b>End point values</b>	Pegcetacoplan 270 mg/day			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: µg/mL				
arithmetic mean (standard deviation)	9999999 (± 9999999)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Area Under the Serum Concentration Versus Time Curve From Time 0 to the Last Measurable Concentration at the End of the Study (AUCtotal)

End point title	Mean Area Under the Serum Concentration Versus Time Curve From Time 0 to the Last Measurable Concentration at the End of the Study (AUCtotal)
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End point description:

The AUC<sub>total</sub> of pegcetacoplan was estimated using a non-compartmental approach. Analysis performed on the PK set consisting of all subjects in the safety set who had at least 1 quantifiable PK sample post dose PK measurement.

Note: 9999999 indicates that a value was not calculated. Although data were collected for this endpoint, due to the small sample size, the individual values were listed and used for graphical presentation per subject over time only and therefore no summary statistics were prepared. Full range AUC<sub>total</sub> of pegcetacoplan: 4850000 to 6910000 hour\*µg/mL.

End point type	Secondary
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End point timeframe:

Blood samples were collected predose and at least 2.5 hours post dose on Day 1 and predose on Days 2 up to Day 365.

<b>End point values</b>	Pegcetacoplan 270 mg/day			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: hour*µg/mL				
arithmetic mean (standard deviation)	9999999 (± 9999999)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Maximum Observed Predose Serum Concentration During the Study (C<sub>trough</sub>,Max,Total)

End point title	Mean Maximum Observed Predose Serum Concentration During the Study (C <sub>trough</sub> ,Max,Total)
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End point description:

The C<sub>trough,max,total</sub> of pegcetacoplan was estimated using a non-compartmental approach. Analysis performed on the PK set consisting of all subjects in the safety set who had at least 1 quantifiable PK sample post dose PK measurement.

Note: 9999999 indicates that a value was not calculated. Although data were collected for this endpoint, due to the small sample size, the individual values were listed and used for graphical presentation per subject over time only and therefore no summary statistics were prepared. Full range C<sub>trough,max,total</sub> of pegcetacoplan: 674 to 912 µg/mL.

End point type	Secondary
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End point timeframe:

Blood samples were collected predose and at least 2.5 hours post dose on Day 1 and predose on Days 2 up to Day 365.

<b>End point values</b>	Pegcetacoplan 270 mg/day			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: µg/mL				
arithmetic mean (standard deviation)	9999999 (± 9999999)			

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

TEAEs were collected from Day 1 up to 30 days after the last dose of study drug (a total of approximately 56 weeks).

Adverse event reporting additional description:

The safety set consisted of all subjects who received at least 1 dose of study drug.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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### Reporting groups

Reporting group title	Pegcetacoplan 270 mg/day
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Reporting group description:

Subjects received SC infusions of pegcetacoplan 270 mg/day up to Day 364. Intrasubject dose escalation up to a dosage of 360 mg/day was permitted if clinically indicated.

<b>Serious adverse events</b>	Pegcetacoplan 270 mg/day		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Pegcetacoplan 270 mg/day		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	3		
General disorders and administration			

site conditions			
Administration site swelling subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Injection site discolouration subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Injection site erythema subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 8		
Injection site pruritus subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Injection site swelling subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 4		
Reproductive system and breast disorders			
Scrotal irritation subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Skin and subcutaneous tissue disorders			
Erythema subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 37		
Infections and infestations			
Rhinitis subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2		

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported