Clinical trial results:
A Phase 3, Randomized, Placebo-Controlled, Double-Blinded, Multicenter Study to Evaluate the Efficacy and Safety of Pegcetacoplan in Patients with C3 Glomerulopathy or Immune-Complex Membranoproliferative Glomerulonephritis

Summary

EudraCT number	2020-003767-25
Trial protocol	DE NL CZ BE AT FR PL IT ES
Global end of trial date	14 January 2025

Results information

Result version number	v1 (current)
This version publication date	27 July 2025
First version publication date	27 July 2025

Trial information

Trial identification

Sponsor protocol code	APL2-C3G-310

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05067127
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Apellis Pharmaceuticals, Inc
Sponsor organisation address	100 5th Ave, 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)	Yes
EMA paediatric investigation plan number(s)	EMEA-002600-PIP04-22
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	14 January 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the efficacy of twice weekly subcutaneous (SC) doses of pegcetacoplan compared with that of placebo in subjects with primary complement 3 glomerulopathy (C3G) or immune-complex membranoproliferative glomerulonephritis (IC-MPGN) on the basis of a reduction in proteinuria.

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 of Technical Requirements for Pharmaceuticals for Human Use Harmonised Guideline for Good Clinical Practice E6 Revision 2. An external, independent data monitoring committee assessed the safety and tolerability data of the study periodically.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 May 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Brazil: 19
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Japan: 3
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Switzerland: 3
Country: Number of subjects enrolled	United Kingdom: 9

Country: Number of subjects enrolled	United States: 31
Worldwide total number of subjects	124
EEA total number of subjects	44

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)	55
Adults (18-64 years)	67
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase 3 randomized, placebo-controlled, double-blinded study was conducted in subjects with C3G or primary IC-MPGN at 122 sites.

Pre-assignment

Screening details:

This study consisted of a screening period (10 weeks), 26-week randomized controlled period (RCP), followed by a 26-week open-label period (OLP) and follow-up period (8 weeks). Subjects were randomized to receive pegcetacoplan or placebo in a ratio of 1:1 in RCP. A total of 124 subjects were enrolled in this study.

Period 1

Period 1 title	Randomized Controlled Period (26 Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Randomized Controlled Period: Pegcetacoplan

Arm description:

All adult subjects (regardless of weight) and adolescent subjects with body weight >=50 kilogram (kg) received pegcetacoplan 1080 milligram (mg) subcutaneous (SC) infusion twice weekly for 26 weeks in RCP.
Adolescent subjects with body weight 35 to <50 kg received pegcetacoplan 648 mg for the first SC infusion and 810 mg SC infusion thereafter twice weekly for 26 weeks in RCP.
Adolescent subjects with body weight 30 to <35 kg received pegcetacoplan 540 mg for the first 2 SC infusions and 648 mg SC infusion thereafter twice weekly for 26 weeks in RCP.

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

Dosage and administration details:

Pegcetacoplan SC infusion twice weekly for 26 weeks in RCP.

Arm title	Randomized Controlled Period: Placebo

Arm description:

All adult subjects (regardless of weight) and adolescent subjects (with body weight: 30 to <35 kg, 35 to <50 kg, and >=50 kg) received placebo matching with pegcetacoplan SC infusion twice weekly for 26 weeks in RCP.

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

Dosage and administration details:

Placebo matching with pegcetacoplan SC infusion twice weekly for 26 weeks in RCP.

Number of subjects in period 1	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo
Started	63	61
Completed	61	57
Not completed	2	4
Consent withdrawn by subject	-	2
Investigator or Medical Monitor Decision	1	-
Death	1	-
Pregnancy	-	1
Lost to follow-up	-	1

Period 2

Period 2 title	Open-Label Period (26 Weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Open-Label Period: Pegcetacoplan to Pegcetacoplan

Arm description:

All eligible adult subjects (regardless of weight) and adolescent subjects with body weight >=50 kg who received pegcetacoplan in RCP continued to receive pegcetacoplan 1080 mg SC infusion twice weekly for 26 weeks in OLP.
Eligible adolescent subjects with body weight 35 to <50 kg who received pegcetacoplan in RCP continued to receive pegcetacoplan 810 mg SC infusion twice weekly for 26 weeks in OLP.
Eligible adolescent subjects with body weight 30 to <35 kg who received pegcetacoplan in RCP continued to receive pegcetacoplan 648 mg SC infusion twice weekly for 26 weeks in OLP.

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

Dosage and administration details:

Pegcetacoplan SC infusion twice weekly for 26 weeks in OLP.

Arm title	Open-Label Period: Placebo to Pegcetacoplan

Arm description:

All eligible adult subjects (regardless of weight) and adolescent subjects with body weight >=50 kg who received placebo in RCP entered OLP to receive pegcetacoplan 1080 mg SC infusion twice weekly for 26 weeks in OLP.
Eligible adolescent subjects with body weight 35 to <50 kg who received placebo in RCP entered OLP to receive pegcetacoplan 810 mg SC infusion twice weekly for 26 weeks in OLP.
Eligible adolescent subjects with body weight 30 to <35 kg who received placebo in RCP entered OLP to

receive pegcetacoplan 648 mg SC infusion twice weekly for 26 weeks in OLP.

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

Dosage and administration details:

Placebo matching with pegcetacoplan SC infusion twice weekly for 26 weeks in OLP.

Number of subjects in period 2	Open-Label Period: Pegcetacoplan to Pegcetacoplan	Open-Label Period: Placebo to Pegcetacoplan
Started	61	57
Completed	59	55
Not completed	2	2
Consent withdrawn by subject	-	1
Investigator or Medical Monitor Decision	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Randomized Controlled Period: Pegcetacoplan
Reporting group description:	
All adult subjects (regardless of weight) and adolescent subjects with body weight >=50 kilogram (kg) received pegcetacoplan 1080 milligram (mg) subcutaneous (SC) infusion twice weekly for 26 weeks in RCP. Adolescent subjects with body weight 35 to <50 kg received pegcetacoplan 648 mg for the first SC infusion and 810 mg SC infusion thereafter twice weekly for 26 weeks in RCP. Adolescent subjects with body weight 30 to <35 kg received pegcetacoplan 540 mg for the first 2 SC infusions and 648 mg SC infusion thereafter twice weekly for 26 weeks in RCP.	
Reporting group title	Randomized Controlled Period: Placebo
Reporting group description:	
All adult subjects (regardless of weight) and adolescent subjects (with body weight: 30 to <35 kg, 35 to <50 kg, and >=50 kg) received placebo matching with pegcetacoplan SC infusion twice weekly for 26 weeks in RCP.	

Reporting group values	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo	Total
Number of subjects	63	61	124
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	28.2	23.6	
standard deviation	± 17.08	± 14.26	-
Gender categorical Units: Subjects			
Female	37	33	70
Male	26	28	54
Race Units: Subjects			
American Indian or Alaskan Native	1	0	1
Asian	9	9	18
Black or African American	1	0	1
White	45	46	91
Other	7	6	13
Ethnicity Units: Subjects			
Hispanic	15	10	25
Not Hispanic or Latino	41	47	88
Not Reported	6	2	8
Unknown	1	2	3

End points

End points reporting groups

Reporting group title	Randomized Controlled Period: Pegcetacoplan

Reporting group description:

All adult subjects (regardless of weight) and adolescent subjects with body weight >=50 kilogram (kg) received pegcetacoplan 1080 milligram (mg) subcutaneous (SC) infusion twice weekly for 26 weeks in RCP.
Adolescent subjects with body weight 35 to <50 kg received pegcetacoplan 648 mg for the first SC infusion and 810 mg SC infusion thereafter twice weekly for 26 weeks in RCP.
Adolescent subjects with body weight 30 to <35 kg received pegcetacoplan 540 mg for the first 2 SC infusions and 648 mg SC infusion thereafter twice weekly for 26 weeks in RCP.

Reporting group title	Randomized Controlled Period: Placebo

Reporting group description:

All adult subjects (regardless of weight) and adolescent subjects (with body weight: 30 to <35 kg, 35 to <50 kg, and >=50 kg) received placebo matching with pegcetacoplan SC infusion twice weekly for 26 weeks in RCP.

Reporting group title	Open-Label Period: Pegcetacoplan to Pegcetacoplan

Reporting group description:

All eligible adult subjects (regardless of weight) and adolescent subjects with body weight >=50 kg who received pegcetacoplan in RCP continued to receive pegcetacoplan 1080 mg SC infusion twice weekly for 26 weeks in OLP.
Eligible adolescent subjects with body weight 35 to <50 kg who received pegcetacoplan in RCP continued to receive pegcetacoplan 810 mg SC infusion twice weekly for 26 weeks in OLP.
Eligible adolescent subjects with body weight 30 to <35 kg who received pegcetacoplan in RCP continued to receive pegcetacoplan 648 mg SC infusion twice weekly for 26 weeks in OLP.

Reporting group title	Open-Label Period: Placebo to Pegcetacoplan

Reporting group description:

All eligible adult subjects (regardless of weight) and adolescent subjects with body weight >=50 kg who received placebo in RCP entered OLP to receive pegcetacoplan 1080 mg SC infusion twice weekly for 26 weeks in OLP.
Eligible adolescent subjects with body weight 35 to <50 kg who received placebo in RCP entered OLP to receive pegcetacoplan 810 mg SC infusion twice weekly for 26 weeks in OLP.
Eligible adolescent subjects with body weight 30 to <35 kg who received placebo in RCP entered OLP to receive pegcetacoplan 648 mg SC infusion twice weekly for 26 weeks in OLP.

Primary: Randomized Controlled Period: Change From Baseline in Log-Transformed Urine Protein-to-Creatinine Ratio (uPCR) at Week 26

End point title	Randomized Controlled Period: Change From Baseline in Log-Transformed Urine Protein-to-Creatinine Ratio (uPCR) at Week 26

End point description:

Baseline uPCR value was calculated as the average of the uPCR measurements from at least 6 of the 9 first-morning spot urine (FMU) samples collected between the start of screening and Day 1, inclusive. The uPCR values used to calculate baseline included those from the samples collected on Day −2, Day −1, and before dosing on Day 1. In situations where less than 6 samples or more than 9 samples were collected, the average of all collected samples was used for baseline derivation. The difference between treatment groups using a composite contrast of equal-weighted average over Weeks 24, 25, and 26 was estimated. The intent-to-treat (ITT) analysis set included all randomized subjects.

End point type	Primary

End point timeframe:

Baseline (Day 1) to Week 26

End point values	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	61		
Units: ratio				
least squares mean (confidence interval 95%)	-1.114 (-1.380 to -0.848)	0.029 (-0.090 to 0.148)		

Statistical analyses

Statistical analysis title	Treatment difference in log-transformed uPCR

Statistical analysis description:

An mixed-effect model for repeated measures (MMRM) included fixed categorical effect for treatment group, visit, disease type, baseline immunosuppressants use, stratification factors, and the visit-by-treatment group interactions as well as the continuous, fixed covariate of baseline log-transformed uPCR, was utilized to analyze the log-transformed ratio of uPCR at Week 26 compared to baseline.

Comparison groups	Randomized Controlled Period: Pegcetacoplan v Randomized Controlled Period: Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	MMRM
Parameter estimate	Difference in LS mean
Point estimate	-1.143
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.436
upper limit	-0.85

Secondary: Randomized Controlled Period: Percentage of Subjects Who Achieved the Composite Renal Endpoint at Week 26

End point title	Randomized Controlled Period: Percentage of Subjects Who Achieved the Composite Renal Endpoint at Week 26

End point description:

Subject who achieved a composite renal endpoint was defined as: (1) a stable or improved estimated glomerular filtration rate (eGFR) compared to baseline (<=15% reduction in eGFR), and (2) a >=50% reduction in uPCR compared to baseline. Percentages are rounded off to the hundredth decimal place. The ITT analysis set included all randomized subjects.

End point type	Secondary

End point timeframe:

Week 26

End point values	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	61		
Units: percentage of subjects				
number (not applicable)	49.21	3.28		

Statistical analyses

Statistical analysis title	Treatment difference in composite renal endpoint

Statistical analysis description:

The logistic model included treatment group as independent variable and adjusted for baseline eGFR values, baseline log-transformed uPCR values, disease type, and stratification factors.

Comparison groups	Randomized Controlled Period: Pegcetacoplan v Randomized Controlled Period: Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	27.516
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.105
upper limit	124.026

Secondary: Randomized Controlled Period: Percentage of Subjects With a Reduction of At Least 50% From Baseline in Urine Protein-to-Creatinine Ratio at Week 26

End point title	Randomized Controlled Period: Percentage of Subjects With a Reduction of At Least 50% From Baseline in Urine Protein-to-Creatinine Ratio at Week 26

End point description:

Baseline uPCR value was calculated as the average of the uPCR measurements from at least 6 of the 9 FMU samples collected between the start of screening and Day 1, inclusive. The uPCR values used to calculate baseline included those from the samples collected on Day −2, Day −1, and before dosing on Day 1. In situations where less than 6 samples or more than 9 samples were collected, the average of all collected samples was used for baseline derivation. Percentages are rounded off to the hundredth decimal place. The ITT analysis set included all randomized subjects.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 26

End point values	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	61		
Units: percentage of subjects				
number (not applicable)	60.32	4.92		

Statistical analyses

Statistical analysis title	Treatment difference in 50% reduction in uPCR
Statistical analysis description:	
The logistic model included treatment group as independent variable and adjusted for baseline log-transformed uPCR values, disease type, and stratification factors.	
Comparison groups	Randomized Controlled Period: Pegcetacoplan v Randomized Controlled Period: Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	30.932
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.401
upper limit	113.897

Secondary: Randomized Controlled Period: Change From Baseline in the C3 Glomerulopathy (C3G) Histologic Index Activity Score at Week 26

End point title	Randomized Controlled Period: Change From Baseline in the C3 Glomerulopathy (C3G) Histologic Index Activity Score at Week 26
End point description:	
The C3G histologic index used to assess disease activity and chronicity in C3G. The C3G total activity score ranges from 0 (worse) to 21 (best). Higher scores indicate better outcome. Baseline was defined as the most recent non-missing measurement prior to taking the first dose of study drug. The ITT analysis set included all randomized subjects. Since adolescents subjects were not required to provide post-screening biopsies, this endpoint was analyzed based on adult subjects only.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Week 26	

End point values	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	34		
Units: units on a scale				
least squares mean (confidence interval 95%)	-3.482 (-4.721 to -2.244)	-2.480 (-3.775 to -1.186)		

Statistical analyses

Statistical analysis title	Treatment difference in C3G histologic index
Statistical analysis description:	
Analysis of covariance (ANCOVA) model included treatment as fixed effect, adjusted for baseline C3G histologic index activity score, disease type, and stratification factors.	
Comparison groups	Randomized Controlled Period: Pegcetacoplan v Randomized Controlled Period: Placebo
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2753
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	-1.002
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.803
upper limit	0.798

Secondary: Randomized Controlled Period: Percentage of Subjects Who Showed Decrease in C3c Staining on Renal Biopsy From Baseline at Week 26

End point title	Randomized Controlled Period: Percentage of Subjects Who Showed Decrease in C3c Staining on Renal Biopsy From Baseline at Week 26
End point description:	
Subject who showed decrease in C3c staining was defined as decrease of at least 2 orders of magnitude of intensity from baseline. Percentages are rounded off to the hundredth decimal place. The ITT analysis set included all randomized subjects. Since adolescents subjects were not required to provide post-screening biopsies, this endpoint was analyzed based on adult subjects only.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Week 26	

End point values	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	34		
Units: percentage of subjects				
number (not applicable)	74.29	11.76		

Statistical analyses

Statistical analysis title	Treatment difference in C3c staining

Statistical analysis description:

The logistic model included treatment group as independent variable and adjusted for baseline C3c staining, disease type, and stratification factors.

Comparison groups	Randomized Controlled Period: Pegcetacoplan v Randomized Controlled Period: Placebo
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	27.392
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.477
upper limit	115.852

Secondary: Randomized Controlled Period: Change From Baseline in Estimated Glomerular Filtration Rate at Week 26

End point title	Randomized Controlled Period: Change From Baseline in Estimated Glomerular Filtration Rate at Week 26

End point description:

Serum samples were collected to determine the eGFR, calculated by using chronic kidney disease-epidemiology collaboration (CKD-EPI) creatinine equation for adults and the Bedside Schwartz equation for adolescents. Baseline eGFR value was calculated using the last non-missing assessment prior to first dose of study drug. The ITT analysis set included all randomized subjects.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 26

End point values	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	61		
Units: milliliter (mL)/minute/1.73 meter square				
least squares mean (confidence interval 95%)	-1.497 (-5.892 to 2.899)	-7.808 (-11.570 to -4.047)		

Statistical analyses

Statistical analysis title	Treatment difference in eGFR
Statistical analysis description:	
An MMRM model included fixed categorical effect for treatment group, visit, disease type, stratification factors, and the visit-by-treatment group interactions as well as the continuous, fixed covariate of baseline eGFR, was utilized to analyze the mean change from baseline to Week 26 in eGFR.	
Comparison groups	Randomized Controlled Period: Pegcetacoplan v Randomized Controlled Period: Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0333
Method	MMRM
Parameter estimate	Difference in LS mean
Point estimate	6.312
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.501
upper limit	12.122

Secondary: Randomized Controlled Period: Percentage of Subjects Who Achieved Proteinuria <1 Gram (g)/Day at Week 24

End point title	Randomized Controlled Period: Percentage of Subjects Who Achieved Proteinuria <1 Gram (g)/Day at Week 24
End point description:	
Urine samples were collected to determine the proteinuria. Percentage of subjects who achieved proteinuria <1 g/day was assessed by 24-hour urine protein. Percentages are rounded off to the hundredth decimal place. The ITT analysis set included all randomized subjects.	
End point type	Secondary
End point timeframe:	
Week 24	

End point values	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	61		
Units: percentage of subjects				
number (not applicable)	36.51	11.48		

Statistical analyses

Statistical analysis title	Treatment difference in proteinuria <1 g/day

Statistical analysis description:

The logistic model included treatment group as independent variable and adjusted for baseline proteinuria values, disease type, and stratification factors.

Comparison groups	Randomized Controlled Period: Pegcetacoplan v Randomized Controlled Period: Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.753
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.106
upper limit	15.716

Secondary: Randomized Controlled Period: Percentage of Subjects With Normalization of Serum Albumin Levels at Week 26

End point title	Randomized Controlled Period: Percentage of Subjects With Normalization of Serum Albumin Levels at Week 26

End point description:

Baseline serum albumin value was calculated as the average of up to 2 serum albumin measurements preceding and including Day 1. Week 26 serum albumin values was calculated as the average of up to 2 serum albumin measurements preceding and including Week 26, no earlier than Week 20 measurement. Percentages are rounded off to the hundredth decimal place. The ITT analysis set included all randomized subjects. Only subjects with serum albumin levels below lower limit of normal (LLN) at baseline are analyzed.

End point type	Secondary

End point timeframe:

Week 26

End point values	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	23		
Units: percentage of subjects				
number (not applicable)	77.78	4.35		

Statistical analyses

Statistical analysis title	Treatment difference in serum albumin levels

Statistical analysis description:

The logistic model included treatment group as independent variable and adjusted for baseline albumin values, disease type, and stratification factors.

Comparison groups	Randomized Controlled Period: Pegcetacoplan v Randomized Controlled Period: Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	88.341
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.863
upper limit	880.544

Secondary: Randomized Controlled Period: Percentage of Subjects With Serum C3 Levels Above the Lower Limit of Normal at Week 26

End point title	Randomized Controlled Period: Percentage of Subjects With Serum C3 Levels Above the Lower Limit of Normal at Week 26

End point description:

Baseline serum C3 value was calculated as the average of up to 2 serum C3 measurements preceding and including Day 1. Week 26 serum C3 value was calculated as the average of up to 2 serum C3 measurements preceding and including Week 26, no earlier than Week 20 measurement. Percentages are rounded off to the hundredth decimal place. The ITT analysis set included all randomized subjects. Only subjects with serum C3 levels below LLN at baseline are analyzed.

End point type	Secondary

End point timeframe:

Week 26

End point values	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	49		
Units: percentage of subjects				
number (not applicable)	90.24	6.12		

Statistical analyses

Statistical analysis title	Treatment difference in serum C3 levels
Statistical analysis description:	
The logistic model included treatment group as independent variable and adjusted for baseline C3 levels, stratification factors and disease type.	
Comparison groups	Randomized Controlled Period: Pegcetacoplan v Randomized Controlled Period: Placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0094
Method	Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	999.999
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.175
upper limit	9999.999

Secondary: Randomized Controlled Period: Change From Baseline in the Functional Assessment of Chronic Illness Therapy- Fatigue (FACIT-Fatigue) Score at Week 26

End point title	Randomized Controlled Period: Change From Baseline in the Functional Assessment of Chronic Illness Therapy- Fatigue (FACIT-Fatigue) Score at Week 26
End point description:	
The FACIT-Fatigue scale was a 13-item Likert scaled instrument that was self-administered by subjects. Subjects were presented with 13 statements and asked to indicate their responses 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 has a range of 0 (worse health-related quality of life) to 52 (best health-related quality of life). Higher scores indicate better quality of life. Baseline was defined as the most recent non-missing measurement prior to taking the first dose of study drug. The ITT analysis set included all randomized subjects.	
End point type	Secondary
End point timeframe:	
Baseline (Day 1) and Week 26	

End point values	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	61		
Units: units on a scale				
least squares mean (confidence interval 95%)	0.929 (-1.549 to 3.407)	0.367 (-1.949 to 2.683)		

Statistical analyses

Statistical analysis title	Treatment difference in FACIT-fatigue score

Statistical analysis description:

The ANCOVA model included treatment as fixed effect, adjusted for baseline, disease type, and stratification factors.

Comparison groups	Randomized Controlled Period: Pegcetacoplan v Randomized Controlled Period: Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7384
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	0.562
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.739
upper limit	3.863

Secondary: Randomized Controlled Period: Change From Baseline in the Kidney Disease Quality of Life (KDQOL) Score at Week 26

End point title	Randomized Controlled Period: Change From Baseline in the Kidney Disease Quality of Life (KDQOL) Score at Week 26

End point description:

The KDQOL score was constructed as the KDQOL-36 Summary Score (KSS) by averaging the 24 items from Burden of Kidney Disease, Symptoms and Problems of Kidney Disease, and Effects of Kidney Disease on scale ranging from 0 (worse health-related quality of life) to 100 (best health-related quality of life). Higher scores indicate better quality of life. Baseline was defined as the most recent non-missing measurement prior to taking the first dose of study drug. The ITT analysis set included all randomized subjects.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 26

End point values	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	61		
Units: units on a scale				
least squares mean (confidence interval 95%)	0.757 (-2.385 to 3.900)	-0.587 (-3.847 to 2.672)		

Statistical analyses

Statistical analysis title	Treatment difference in KDQOL score
Statistical analysis description:	
The ANCOVA model included treatment as fixed effect, adjusted for baseline, disease type, and stratification factors.	
Comparison groups	Randomized Controlled Period: Pegcetacoplan v Randomized Controlled Period: Placebo
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5648
Method	ANCOVA
Parameter estimate	Difference in LS mean
Point estimate	1.345
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.237
upper limit	5.927

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAE data is reported from first dose of study drug (Day 1) up to 56 days after the last dose of study drug (Week 52), up to 60 weeks.
Deaths (all-cause): From first dose of study drug (Day 1) up to end of the study, approximately 137 weeks.

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Randomized Controlled Period: Pegcetacoplan

Reporting group description:

All adult subjects (regardless of weight) and adolescent subjects with body weight >=50 kg received pegcetacoplan 1080 mg SC infusion twice weekly for 26 weeks in RCP.
Adolescent subjects with body weight 35 to <50 kg received pegcetacoplan 648 mg for the first SC infusion and 810 mg SC infusion thereafter twice weekly for 26 weeks in RCP.
Adolescent subjects with body weight 30 to <35 kg received pegcetacoplan 540 mg for the first 2 SC infusions and 648 mg SC infusion thereafter twice weekly for 26 weeks in RCP.

Reporting group title	Randomized Controlled Period: Placebo

Reporting group description:

All adult subjects (regardless of weight) and adolescent subjects (with body weight: 30 to <35 kg, 35 to <50 kg, and >=50 kg) received placebo matching with pegcetacoplan SC infusion twice weekly for 26 weeks in RCP.

Reporting group title	Open-Label Period: Pegcetacoplan to Pegcetacoplan

Reporting group description:

All eligible adult subjects (regardless of weight) and adolescent subjects with body weight >=50 kg who received pegcetacoplan in RCP continued to receive pegcetacoplan 1080 mg SC infusion twice weekly for 26 weeks in OLP.
Eligible adolescent subjects with body weight 35 to <50 kg who received pegcetacoplan in RCP continued to receive pegcetacoplan 810 mg SC infusion twice weekly for 26 weeks in OLP.
Eligible adolescent subjects with body weight 30 to <35 kg who received pegcetacoplan in RCP continued to receive pegcetacoplan 648 mg SC infusion twice weekly for 26 weeks in OLP.

Reporting group title	Open-Label Period: Placebo to Pegcetacoplan

Reporting group description:

All eligible adult subjects (regardless of weight) and adolescent subjects with body weight >=50 kg who received placebo in RCP entered OLP to receive pegcetacoplan 1080 mg SC infusion twice weekly for 26 weeks in OLP.
Eligible adolescent subjects with body weight 35 to <50 kg who received placebo in RCP entered OLP to receive pegcetacoplan 810 mg SC infusion twice weekly for 26 weeks in OLP.
Eligible adolescent subjects with body weight 30 to <35 kg who received placebo in RCP entered OLP to receive pegcetacoplan 648 mg SC infusion twice weekly for 26 weeks in OLP.

Serious adverse events	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo	Open-Label Period: Pegcetacoplan to Pegcetacoplan
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 63 (9.52%)	6 / 61 (9.84%)	6 / 61 (9.84%)
number of deaths (all causes)	1	0	0
number of deaths resulting from	1	0	0

adverse events			
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	0 / 61 (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
Injury, poisoning and procedural complications			
Maternal exposure during pregnancy			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	0 / 61 (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
Post procedural haematoma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt malfunction			
subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt thrombosis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	0 / 61 (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
Hypertensive urgency			
subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	0 / 61 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	0 / 61 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	0 / 61 (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
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 63 (1.59%)	2 / 61 (3.28%)	2 / 61 (3.28%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
End stage renal disease			

subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	0 / 61 (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
Renal failure			
subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	0 / 61 (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
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	0 / 61 (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
Gastroenteritis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster meningoencephalitis			

subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	0 / 61 (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
Pneumonia			
subjects affected / exposed	1 / 63 (1.59%)	0 / 61 (0.00%)	0 / 61 (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
Pneumonia pneumococcal			
subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shunt infection			
subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 63 (0.00%)	0 / 61 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Open-Label Period: Placebo to Pegcetacoplan		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 57 (7.02%)		
number of deaths (all causes)	0		
number of deaths resulting from	0		

adverse events			
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 57 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Maternal exposure during pregnancy			
subjects affected / exposed	0 / 57 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural haematoma			
subjects affected / exposed	0 / 57 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Shunt malfunction			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shunt thrombosis			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 57 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive urgency			
subjects affected / exposed	0 / 57 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			

subjects affected / exposed	0 / 57 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 57 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 57 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 57 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
End stage renal disease			

subjects affected / exposed	0 / 57 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrotic syndrome				
subjects affected / exposed	0 / 57 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proteinuria				
subjects affected / exposed	0 / 57 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 57 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	0 / 57 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tubulointerstitial nephritis				
subjects affected / exposed	0 / 57 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
COVID-19 pneumonia				
subjects affected / exposed	0 / 57 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster meningoencephalitis				

subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 57 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 57 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia pneumococcal				
subjects affected / exposed	0 / 57 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Shunt infection				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	0 / 57 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	1 / 57 (1.75%)			
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	Randomized Controlled Period: Pegcetacoplan	Randomized Controlled Period: Placebo	Open-Label Period: Pegcetacoplan to Pegcetacoplan
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 63 (84.13%)	56 / 61 (91.80%)	47 / 61 (77.05%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	4 / 63 (6.35%)	1 / 61 (1.64%)	0 / 61 (0.00%)
occurrences (all)	4	2	0
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 63 (4.76%)	5 / 61 (8.20%)	6 / 61 (9.84%)
occurrences (all)	5	5	6
Hypotension			
subjects affected / exposed	2 / 63 (3.17%)	0 / 61 (0.00%)	0 / 61 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 63 (0.00%)	6 / 61 (9.84%)	3 / 61 (4.92%)
occurrences (all)	0	6	3
Headache			
subjects affected / exposed	8 / 63 (12.70%)	11 / 61 (18.03%)	4 / 61 (6.56%)
occurrences (all)	20	14	7
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 63 (0.00%)	4 / 61 (6.56%)	5 / 61 (8.20%)
occurrences (all)	0	4	5
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 63 (0.00%)	4 / 61 (6.56%)	0 / 61 (0.00%)
occurrences (all)	0	4	0
Fatigue			
subjects affected / exposed	4 / 63 (6.35%)	1 / 61 (1.64%)	2 / 61 (3.28%)
occurrences (all)	4	1	2
Infusion site erythema			
subjects affected / exposed	4 / 63 (6.35%)	1 / 61 (1.64%)	0 / 61 (0.00%)
occurrences (all)	4	1	0
Infusion site pain			

subjects affected / exposed	1 / 63 (1.59%)	4 / 61 (6.56%)	0 / 61 (0.00%)
occurrences (all)	1	5	0
Infusion site swelling			
subjects affected / exposed	0 / 63 (0.00%)	1 / 61 (1.64%)	1 / 61 (1.64%)
occurrences (all)	0	2	1
Injection site pain			
subjects affected / exposed	2 / 63 (3.17%)	5 / 61 (8.20%)	0 / 61 (0.00%)
occurrences (all)	2	11	0
Injection site swelling			
subjects affected / exposed	2 / 63 (3.17%)	7 / 61 (11.48%)	1 / 61 (1.64%)
occurrences (all)	33	48	44
Oedema			
subjects affected / exposed	3 / 63 (4.76%)	5 / 61 (8.20%)	1 / 61 (1.64%)
occurrences (all)	4	6	1
Pyrexia			
subjects affected / exposed	12 / 63 (19.05%)	7 / 61 (11.48%)	5 / 61 (8.20%)
occurrences (all)	14	7	7
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 63 (6.35%)	4 / 61 (6.56%)	2 / 61 (3.28%)
occurrences (all)	6	5	2
Diarrhoea			
subjects affected / exposed	2 / 63 (3.17%)	7 / 61 (11.48%)	4 / 61 (6.56%)
occurrences (all)	3	8	5
Nausea			
subjects affected / exposed	6 / 63 (9.52%)	4 / 61 (6.56%)	6 / 61 (9.84%)
occurrences (all)	8	4	10
Vomiting			
subjects affected / exposed	5 / 63 (7.94%)	9 / 61 (14.75%)	7 / 61 (11.48%)
occurrences (all)	7	13	10
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 63 (9.52%)	1 / 61 (1.64%)	4 / 61 (6.56%)
occurrences (all)	7	1	5
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	0 / 63 (0.00%)	4 / 61 (6.56%)	0 / 61 (0.00%)
occurrences (all)	0	4	0
Pruritus			
subjects affected / exposed	2 / 63 (3.17%)	0 / 61 (0.00%)	4 / 61 (6.56%)
occurrences (all)	2	0	4
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 63 (0.00%)	4 / 61 (6.56%)	1 / 61 (1.64%)
occurrences (all)	0	4	1
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 63 (3.17%)	4 / 61 (6.56%)	3 / 61 (4.92%)
occurrences (all)	2	4	3
Influenza			
subjects affected / exposed	6 / 63 (9.52%)	3 / 61 (4.92%)	4 / 61 (6.56%)
occurrences (all)	6	4	4
Nasopharyngitis			
subjects affected / exposed	11 / 63 (17.46%)	7 / 61 (11.48%)	7 / 61 (11.48%)
occurrences (all)	15	8	9
Upper respiratory tract infection			
subjects affected / exposed	4 / 63 (6.35%)	5 / 61 (8.20%)	4 / 61 (6.56%)
occurrences (all)	4	5	5

Non-serious adverse events	Open-Label Period: Placebo to Pegcetacoplan		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 57 (73.68%)		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Hypotension			

subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	4		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 57 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	7 / 57 (12.28%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 57 (7.02%)		
occurrences (all)	4		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Infusion site erythema			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	54		
Infusion site pain			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	3		
Infusion site swelling			
subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	3		
Injection site pain			
subjects affected / exposed	0 / 57 (0.00%)		
occurrences (all)	0		
Injection site swelling			
subjects affected / exposed	4 / 57 (7.02%)		
occurrences (all)	22		
Oedema			

subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	4 / 57 (7.02%)		
occurrences (all)	4		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	8 / 57 (14.04%)		
occurrences (all)	9		
Nausea			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	5		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 57 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19			

subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 March 2021	Updated study design so that the RCP was double-blinded and added justification of study design section. Shortened the follow-up period for subjects who did not continued receiving pegcetacoplan from 24 to 8 weeks. Added an interim analysis of efficacy when all subjects had completed the 26-week RCP. Revised the endpoints. Amended inclusion and exclusion criteria. Revised dosing recommendations, added regimens for adolescent subjects >=50 kg, 35 to <50 kg, and 20 to <35 kg. Update wording describing monitoring and reporting of AEs and SAEs to align with current company practices. Added wording describing risks related coronavirus disease 2019 (COVID-19) and activities to mitigate these risks.
14 August 2021	Changed planned enrollment from 90 to 80-100 subjects. Clarified vaccination strategy and prophylactic antibiotic use in Risk/Benefit discussion. Changed primary and key secondary objectives to align with endpoint changes. Changed primary efficacy endpoint to remove eGFR component. Changed primary and key secondary efficacy endpoints from Week 52 to Week 26. Increased minimum body weight to 30 kg. Removed discussion of extrapolating placebo response rate from Week 26 to Week 52. Removed interim analyses (interim analysis 1 for sample size readjustment and interim analysis 2 for early efficacy assessment). Added COVID-19 vaccine to COVID-19 risk mitigation section and COVID-19 Appendix.
03 March 2023	Increased duration of screening period from 8 to 10 weeks with a corresponding increase of total duration of study participation to 70 weeks. Increased the minimum number of adolescent participants from 8 to 10. Revised endpoints. Updated discussion of the determination of sample size. Updated the discussion of the efficacy analyses. Updated discussion of assessment of severity of AEs.
25 April 2024	Order of key secondary endpoints revised. Removed exploratory endpoint evaluating normalization of hematuria. Removed exploratory endpoint of evaluation of changes in drusen at 26 weeks. Revised description of the data review for the analysis set. Added description of the activities at the closure of enrollment. Revised description of antidrug antibody assessments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported