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

Published: 13-10-2021
Last updated: 10-01-2025

This study has been transitioned to CTIS with ID 2024-514130-20-00 check the CTIS register for the current data. The primary objective of this study is to assess the efficacy of twice-weekly SC doses of pegcetacoplan compared with that of placebo in…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON55956

Source
ToetsingOnline

Brief title
VALIANT

Condition

- Nephropathies

Synonym
glomerulus diseases, kidney diseases

Research involving
Human

Sponsors and support

Primary sponsor: Apellis Pharmaceuticals, Inc
Source(s) of monetary or material Support: Apellis Pharmaceuticals;Inc

Intervention

Keyword: glomerulonephritis, glomerulopathy, pegcetacoplan

Outcome measures

Primary outcome

The primary efficacy endpoint is the log-transformed ratio of urine

protein-to-creatinine ratio (uPCR) at Week 26 compared to baseline.

Secondary outcome

The key secondary efficacy endpoints at week 26:

• The proportion of participants who meet the criteria for achieving a

composite renal endpoint (a stable or improved eGFR compared to the baseline

visit (<=15% reduction in eGFR), and a >=50% reduction in uPCR compared to the

baseline visit.)

• The proportion of participants with reductions of at least 50% from baseline

in uPCR

• For participants with evaluable renal biopsies, the change from baseline in

the activity score of the C3G histological activity index score

• The proportion of participants with evaluable renal biopsies showing

decreases in C3c staining from baseline

Additional secondary efficacy endpoints (to be Evaluated at Week 26):

• Change from baseline in eGFR

• The proportion of participants achieving proteinuria <1 g/day

• For participants with serum albumin levels below the lower limit of normal

(LLN) at baseline, the proportion of participants with normalization of serum

albumin levels

• For participants with serum C3 levels below LLN at baseline, the proportion

of participants with normalization of serum C3 levels above the LLN

• The log-transformed ratio of uPCR at week 52 compared to baseline

• The change from baseline in the Kidney Disease Quality of Life (KDQOL) score

Study description

Background summary

C3G and IC-MPGN are rare, chronic diseases that are a result of uncontrolled or improper activation of part of the immune system called the complement system. In people with C3G or IC-MPGN, a protein called complement C3 is over-activated, and can cause kidney damage when its breakdown products form harmful deposits in the kidney. Over time, this stops the kidneys from removing waste in the blood. This waste, if not removed from the blood, builds up in the body and may lead to kidney failure. Symptoms associated with damaged kidneys include blood and protein in urine, high blood pressure, and water retention (swelling).
In this research study an investigational medication named pegcetacoplan (peg-set-a-koé-plan) is being tested for the treatment of C3G or IC-MPGN. Pegcetacoplan inhibits the C3 protein in the complement system, so this study will help us find out if this action can slow or reduce kidney damage. Under normal conditions, the complement system will help remove pathogens and damaged cells without hurting the body. However, sometimes uncontrolled or improper activation of the complement system can damage the body.

Study objective

This study has been transitioned to CTIS with ID 2024-514130-20-00 check the CTIS register for the current data.

The primary objective of this study is to assess the efficacy of twice-weekly SC doses of pegcetacoplan compared with that of placebo in patients with primary C3G or IC-MPGN on the basis of a reduction in proteinuria in the setting of stable or improved eGFR.

Secondary Objectives
• To assess the effect of pegcetacoplan on estimated glomerular filtration rate (eGFR)
• To assess the effect of pegcetacoplan on additional C3G/IC-MPGN disease-related parameters
• To evaluate the safety of pegcetacoplan over 52 weeks of treatment

Study design

This is a Phase 3, randomized, placebo-controlled, double-blinded, multicenter study to evaluate the safety and efficacy of twice-weekly SC infusions of pegcetacoplan in patients diagnosed with primary C3G or IC-MPGN.

The planned duration of participation in the study for each participant is up to approximately 70 weeks. The study will consist of 4 parts:
• Part 1: up to 10-week screening period
• Part 2: 26-week randomized controlled period (RCP)
• Part 3: 26-week open-label period
• Part 4: 8-week follow-up period (only for participants who do not roll into a long-term extension study)

Intervention

All participants will receive SC infusions of pegcetacoplan or matching volumes of placebo twice weekly. The planned dosing regimens for pegcetacoplan and the matching volume of placebo. All adult participants (regardless of weight) and adolescent participants who weigh at least 50 kg will receive 20-mL SC infusions. Adolescent participants who weigh at least 35 kg but less than 50 kg will receive a reduced infusion volume (12 mL for the first infusion and 15 mL for each infusion thereafter). Adolescent participants who weigh at least 30 kg but less than 35 kg will receive a further reduced infusion volume (10 mL for the first 2 infusions and 12 mL twice weekly thereafter). Participant weight will be assessed at each visit; if an adolescent subject*s weight has changed, the dose and infusion volume should be adjusted accordingly.

Study burden and risks

Pegcetacoplan has the potential to address the underlying disease pathophysiology of complement hyperactivity in C3G and IC-MPGN, and, therefore, to provide benefit in these diseases with a high unmet medical need.
The safety of SC pegcetacoplan administration has been studied in multiple

Phase 2 and 3 studies for C3G, PNH, and autoimmune hemolytic anemia, with an acceptable safety profile to date. Nonetheless, a number of safety monitoring practices are being employed by this protocol to ensure participant safety, including physical examination, vital signs monitoring, electrocardiograms (ECGs), hematology (including coagulation), serum chemistry, urinalysis at specified intervals, as well as prompt reporting of adverse events (AEs). Infusion site/pump safety will be assessed during clinical visits, and any significant finding from the assessment will be recorded as an AE. The volume of blood planned for collection from each participant over the course of the study will be minimized in order to limit the impact on the overall health of these anemic participants.
Systemic complement inhibition might predispose individuals to infections caused by encapsulated organisms, including Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae. Vaccinations against these organisms according to the most current Advisory Committee on Immunization Practices (ACIP) recommendations for patients with complement deficiencies will be required to minimize potential risk of infection. Vaccinations will be initiated at least 2 weeks prior to receiving the first dose of pegcetacoplan; therefore, prophylactic antibiotic use is not required. Body temperature and vital signs will be monitored periodically, and relevant blood parameters monitored regularly throughout the study to assess for signs of infection. Participants will be counseled regarding this potential risk for infection and given a patient safety wallet card in the event of an emergency. The investigator should be contacted immediately in the event of a suspected infection for guidance on appropriate action to be taken.
Apellis is not currently aware of any evidence associating pegcetacoplan use with specific risks or complications of coronavirus disease 2019 (COVID-19). Apellis recognizes the need to consider the public health risks of the COVID-19 pandemic within the context of conducting a clinical trial. Because these risks may change as the pandemic evolves and may vary on the basis of geography location, Apellis will continue to evaluate the risk/benefit around study conduct on an ongoing and participant-by-participant basis.

Contacts

Public
Apellis Pharmaceuticals, Inc

5th Avenue, 3rd Floor 100
Waltham MA 02451
US
Scientific
Apellis Pharmaceuticals, Inc

5th Avenue, 3rd Floor 100
Waltham MA 02451
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Aged at least 18 years; where approved, adolescents (aged 12-17 years) weighing at least 30 kg
may also be enrolled.
2. A diagnosis of primary C3G or IC-MPGN (with or without previous renal transplant).
3. Evidence of active renal disease, based on one or more of the following:
a. In adults or adolescents with a baseline renal biopsy (either one collected during screening or a historic biopsy collected within 28 weeks prior to randomization), at least 2+ C3c staining on the baseline renal biopsy.
b. In adolescents not providing a baseline renal biopsy, at least one of the following:
- Plasma sC5b-9 level above the upper limit of normal during screening
- Serum C3 below the LLN during screening
- Presence of an active urine sediment during screening, as evidenced by hematuria with at least 5 red blood cells per high-power field and/or red blood cell casts on routine local or central microscopic analysis of urine
- Presence of C3 nephritic factor within 6 months of screening, based on central laboratory results or medical history
4. No more than 50% global glomerulosclerosis or interstitial fibrosis on the baseline biopsy for adult participants or adolescent participants providing a baseline biopsy.
5. At least 1 g/day of proteinuria on a screening 24-hour urine collection and

a uPCR of at least 1000 mg/g in at least 2 first-morning spot urine samples collected during screening.
6. eGFR >=30 mL/min/1.73 m2 calculated by the Chronic Kidney Disease-Epidemiology Collaboration creatinine equation for adults or the Bedside Schwartz equation for adolescents.
7. Stable regimen for C3G/IC-MPGN treatment, as described below:
a. Angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, and/or sodium-glucose cotransporter-2 inhibitor therapy that is stable and optimized, in the opinion of the investigator, for at least 12 weeks prior to randomization
b. Stable doses of other medications that can affect proteinuria (eg, steroids, mycophenolate mofetil, and/or other allowed immunosuppressants that the participant is receiving for treatment of C3G or IC-MPGN) for at least 12 weeks prior to randomization.
c. If a participant is on prednisone (or other systemic corticosteroid) for C3G or IC-MPGN treatment, the dosage is stable and no higher than 20 mg/day (or equivalent dosage of a corticosteroid other than prednisone) for at least 12 weeks prior to randomization.
8. Have received vaccinations against S pneumoniae, N meningitidis (types A, C, W, Y, and B), and H influenzae (type B) as per ACIP recommendations for adults or children with complement deficiencies. Vaccination series should be initiated at least 14 days prior to randomization. Vaccination is mandatory unless documented evidence exists that participants are nonresponders to vaccination.
9. Female participants of childbearing potential, defined as any women who have experienced menarche and who are not permanently sterile or postmenopausal, must have negative blood pregnancy tests at screening (and negative urine pregnancy tests on Day 1) and must agree to use protocol-defined methods of contraception from screening through at least 90 days after receiving the last dose of pegcetacoplan.
10. Male participants must agree to use protocol-defined methods of contraception and agree to refrain from donating semen from screening through at least 90 days after receiving the last dose of pegcetacoplan.
11. Participants above the legal age of consent, in accordance with local regulations, must be willing and able to provide informed consent. The legally authorized representative of participants under the legal age of consent must be willing and able to provide informed consent; where appropriate, participants under the legal age of consent must also give their assent to participation in the study.
12. Willing and able to self-administer pegcetacoplan or have an identified caregiver who can perform the administration.

Exclusion criteria

1. Previous exposure to pegcetacoplan.

2. Evidence of improving renal disease in the 8 weeks prior to screening or during the screening period according to available data; improving renal disease is defined as >30% increase in eGFR or >50% decrease in proteinuria.
3. From a renal transplant subject, evidence of rejection that requires treatment in the baseline renal biopsy collected during screening.
4. C3G/IC-MPGN secondary to another condition (eg, infection, malignancy, monoclonal gammopathy, a systemic autoimmune disease such as systemic lupus erythematosus, chronic antibody-mediated rejection, or a medication), in the opinion of the investigator.
5. Current or prior diagnosis of HIV, hepatitis B, or hepatitis C infection or positive serology during screening that is indicative of infection with any of these viruses.
6. Weight more than 100 kg at screening.
7. Hypersensitivity to pegcetacoplan or to any of the excipients.
8. History of meningococcal disease.
9. Malignancy, except for the following:
a. Cured basal or squamous cell skin cancer
b. Curatively treated in situ disease
c. Malignancy-free and off treatment for >=5 years
10. Severe infection (eg, requiring IV antibiotic therapy) within 14 days prior to the first dose of pegcetacoplan.
11. An absolute neutrophil count <1000 cells/mm3 at screening
12. Significant other renal disease that would, in the opinion of the investigator, confound interpretation of study results.
13. Participation in any other investigational drug trial or exposure to other investigational agent, device, or procedure within 30 days or 5 half-lives from the last dose of investigational agent (whichever is longer) prior to screening period.
14. Use of rituximab, belimumab, or any approved or investigational anticomplement therapy other than pegcetacoplan within 5 half-lives of that product prior to the screening period.
15. Female participants who are pregnant or who are currently breastfeeding and are unwilling to discontinue for the duration of the study and for at least 90 days after the final dose of study drug.
16. Inability to cooperate or any condition that, in the opinion of the investigator, creates an undue risk for the participant by participating in the study or is likely to confound interpretation of the study results.
17. Evidence of ongoing drug or alcohol abuse or dependence, in the opinion of the investigator.
18. Presence or suspicion of severe infection during the screening period (including but not limited to recurrent) or chronic infections that, in the opinion of the investigator, may place the participant at unacceptable risk by study participation.
19. Known or suspected hereditary fructose intolerance.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-12-2022
Enrollment:	5
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	pegcetacoplan
Generic name:	-

Ethics review

Approved WMO Date:	13-10-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-02-2022
Application type:	First submission

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-02-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-04-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-05-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-05-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-07-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-08-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-10-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-10-2022
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-11-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-12-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-01-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-04-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-06-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-08-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-08-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-12-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-01-2024
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-06-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-06-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-07-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-09-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2024-514130-20-00
EudraCT	EUCTR2020-003767-25-NL
CCMO	NL77632.091.21