AN OPEN-LABEL, RANDOMIZED, CONTROLLED, PHASE 2 STUDY TO EVALUATE THE SAFETY AND EFFICACY OF PEGCETACOPLAN IN THE TREATMENT OF POST-TRANSPLANT RECURRENCE OF C3G OR IC*MPGN

Published: 04-01-2021
Last updated: 10-01-2025

This study has been transitioned to CTIS with ID 2024-511544-36-00 check the CTIS register for the current data. Primary:To evaluate the efficacy of pegcetacoplan in improving the underlying pathophysiology of complement 3 glomerulopathy (C3G)/...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON52109

Source
ToetsingOnline

Brief title
NOBLE

Condition

- Immune disorders NEC

Synonym
Post-Transplant Recurrence

Research involving

Human

Sponsors and support

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

Intervention

Keyword: C3G or IC□MPGN, Pegcetacoplan

Outcome measures

Primary outcome

Primary Efficacy Endpoint:

The primary efficacy endpoint is the proportion of subjects with reduction in

C3c staining on renal biopsy after 12 weeks of treatment with pegcetacoplan.

Secondary outcome

Secondary Efficacy endpoints:

• The proportion of subjects with reduction in C3c staining on renal biopsy

after 52 weeks of treatment

• The proportion of subjects with stabilization or improvement in estimated

glomerular filtration rate (eGFR), over time

• The proportion of subjects with stabilization or improvement in serum

creatinine concentration, over time

• Changes from baseline biopsy in C3c staining over time

• Changes and percentage changes from baseline in eGFR and serum creatinine

concentration over time

Study description

Background summary

There are no therapies approved to prevent or reverse disease progression in C3G or IC-MPGN.
Similar to other glomerular diseases, disease management includes nonspecific measures to
manage proteinuria, hypertension, hyperlipidemia, edema, and other facets of glomerular and chronic kidney disease. Despite these various measures, the prognosis of C3G and IC-MPGN is poor as patients can progress to ESRD.
Renal transplantation is an option for patients who reach ESRD, but the incidence of disease
recurrence is high, with up to 50% of patients losing their renal allografts due to disease
recurrence. Therefore, a therapy that can protect the kidneys, native or transplanted, from ongoing
damage due to complement hyperactivity would be highly desirable. An ongoing study, APL2-201, is studying pegcetacoplan in patients with C3G who have not undergone a renal transplant. Preliminary data from the APL2-201 study indicate that pegcetacoplan is able to target the complement hyperactivity of C3G. The sponsor now aims to study the safety and efficacy of pegcetacoplan in patients with recurrence of C3G or IC-MPGN in a renal allograft.
This study will explore the safety and biologic activity of pegcetacoplan in patients with C3G or
IC-MPGN recurrence post-transplantation. Renal biopsies will be obtained at multiple time
points to assess the ability of pegcetacoplan to reduce the amount of C3c glomerular deposition,
one of the histologic hallmarks of these diseases. This finding, along with increases in intact
serum C3, would provide strong evidence that pegcetacoplan is addressing the underlying
pathophysiology of the disease by preventing excessive production of C3 breakdown products,
and their subsequent deposition into the kidney.

Study objective

This study has been transitioned to CTIS with ID 2024-511544-36-00 check the CTIS register for the current data.

Primary:
To evaluate the efficacy of pegcetacoplan in improving the underlying pathophysiology of complement 3 glomerulopathy (C3G)/immune complex membranoproliferative glomerulonephritis (IC-MPGN) after 12 weeks of treatment.

Secondary:
• To evaluate the effect of pegcetacoplan on key clinical manifestations of the disease after 52 weeks of treatment.
• To evaluate the safety of pegcetacoplan for up to 52 weeks in patients with recurrent C3G/IC-MPGN in a renal allograft.

Study design

This Phase 2, multicenter, open-label, randomized, controlled study is designed to evaluate the safety and efficacy of pegcetacoplan in patients who have post-transplant recurrence of C3G or IC-MPGN. There will be up to 12 patients enrolled in this study. There are 3 periods of this study:
Part A, Core Study:
• Screening period: up to an 8-week week screening period, during which a screening renal allograft biopsy will occur
• Main period: a 52-week study period that contains 2 portions (Controlled and Noncontrolled) during which patients will be randomized to either Group 1 or Group 2 at the Week 1 study visit:
- Controlled portion: Weeks 1-12 of the study
- Group 1: Up to 9 patients will be randomized to this treatment group and will receive pegcetacoplan treatment throughout the entire study; biopsies will occur at Week 12.
- Group 2: Up to 3 patients will be randomized to this treatment group and they will not receive pegcetacoplan treatment during the Controlled Portion; biopsies will occur at Week 12.- Noncontrolled portion: Weeks 13-52 of the study
- Group 1: Patients will continue to receive pegcetacoplan treatment; biopsies will occur at Week 52.
- Group 2: Patients will receive pegcetacoplan treatment following their Week 12 renal allograft biopsy; biopsies will occur at Week 52.
• Follow-up period: a 8-week follow-up period
Part B, Long-Term Extension:
Any patient who, in the opinion of the investigator, is experiencing clinical benefit from pegcetacoplan administration may participate in Part B, a long-term extension, in order to continue to receive treatment with pegcetacoplan until it is commercially available for the disease under study. If invited to participate, the patient can enter Part B as soon as their 52-week treatment period has ended and does not need to participate in the 8-week follow-up period.

Intervention

• Investigational product, pegcetacoplan, will be administered as a 20-mL SC infusion. Subjects will be trained on how to properly store, prepare, and administer pegcetacoplan by the study team during your first 2 infusions. There would be agreement on a dosing schedule with the study doctor, administering

pegcetacoplan on the same days, twice a week (for example, every Tuesday and Friday) for the duration of the study. Additional instructions will be available, and the study team will continue to assist subjects as needed. The study center will supply pegcetacoplan which will need to be kept refrigerated. Additionally, the study center will provide with all other supplies.

Participants will be required to be vaccinated as follows on the basis of Advisory Committee on
Immunization Practices (ACIP) recommendations for adults with complement deficiencies
and/or immunocompromising conditions .
• N. meningitidis types A, C, W, and Y: First dose at least 2 weeks prior to start of
pegcetacoplan with second dose 2 months later, and then boosters every 5 years.
• N. meningitidis type B (Bexsero): First dose at least 2 weeks prior to start of
pegcetacoplan with a second dose after at least 1 month. First booster dose 1 year
later, and then additional booster doses every 2 to 3 years.
• S. pneumoniae: PCV13 and/or PPSV23 as per ACIP guidelines for adults with immunocompromising conditions.

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 subcutaneous pegcetacoplan administration has been studied in multiple Phase 2
and 3 studies for C3G and PNH, with an acceptable safety profile to date. Nonetheless, a number
of safety monitoring practices are being employed by this protocol to ensure patient safety,
including physical examination, vital signs monitoring, electrocardiograms (ECGs), hematology
(including coagulation), serum chemistry, and 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 reported as an AE. The volume of blood planned for collection from each patient over the course of the study will be minimized in order to limit the
impact on the overall health of these anemic patients.

Systemic complement inhibition might predispose individuals to infections caused by
encapsulated organisms, including Streptococcus pneumoniae, Neisseria meningitidis, and
Haemophilus influenzae. Vaccinations against these organisms will be taken to minimize
potential risk of infection. Use of prophylactic antibiotics is allowed, at the discretion of the
investigator, and should take into consideration the level of immunosuppression, complement
levels, and timing of vaccination relative to pegcetacoplan start, as well as local practices. Body
temperature and vital signs will be monitored periodically, and relevant blood parameters
monitored regularly throughout the study to assess for signs of infection. The patient 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 based on
geographic location, Apellis will continue to evaluate the risks and benefits around study conduct
on an ongoing and patient-by-patient basis.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Individuals must meet all of the following criteria at screening visits to be included in the study:
1. At least 18 years of age at screening
2. Must have clinical and pathologic evidence of recurrent C3G or IC-MPGN, as evidenced by all of the following:
a. A diagnosis of C3G or IC-MPGN, with at least 2+ staining for C3c in the renal allograft, confirmed by a central pathologist, based on the screening renal allograft biopsy

b. C3G or IC-MPGN must be primary and not secondary to another condition (eg, infection, malignancy, monoclonal gammopathy, autoimmunity, chronic antibody-mediated rejection, chronic thrombotic microangiopathy, or a medication)
3. Stable (not improving) or worsening disease, in the opinion of the investigator, in the 2 months preceding the first dose of pegcetacoplan
4. eGFR >=15 mL/min/1.73 m2, calculated by the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) creatinine equation for adults
5. No more than 50% glomerulosclerosis or interstitial fibrosis on the screening renal biopsy
6. Stable regimen for recurrent C3G/IC-MPGN for at least 4 weeks prior to the screening renal allograft biopsy and from the time of the screening renal allograft biopsy until randomization
7. Have required vaccinations against N. meningitides, S. pneumoniae, and H. influenzae(type B) or agree to receive vaccinations if applicable vaccination records are not available. Vaccination is mandatory unless documented evidence

exists that subjects are nonresponders to vaccination.
8. Women of childbearing potential, defined as any women who have experienced menarche and who are not permanently sterile or postmenopausal, must have a negative blood pregnancy test at screening (and negative urine pregnancy at Visit 4) and must agree to use protocol defined methods of contraception from screening through 12 weeks after receiving last dose of pegcetacoplan
9. Men must agree to use protocol-defined methods of contraception and agree to refrain from donating semen from screening through 12 weeks after receiving last dose of pegcetacoplan
10. Willing and able to provide written informed consent
11. Able to understand and willing to comply with all scheduled procedures and other requirements of the study in the opinion of the investigator
12. Willing and able to self-administer pegcetacoplan or have an identified caregiver who can perform the administration

Exclusion criteria

Individuals meeting any of the following criteria at screening or baseline are ineligible to participate in this study:
1. Absolute neutrophil count <1000 cells/mm3 during screening (not including Day 1)
2. Previous treatment with pegcetacoplan
3. Evidence of rejection on the screening renal allograft biopsy that requires treatment
4. Diagnosis or history of HIV, hepatitis B, or hepatitis C infection or positive serology at screening indicative of infection with any of these viruses.
5. Weight more than 100 kg at screening
6. Hypersensitivity to pegcetacoplan or any of the excipients
7. History of menigococcal disease
8. 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
9. Significant renal disease in the renal allograft secondary to another condition (eg, infection, malignancy, monoclonal gammopathy, rejection, or a medication) that would , in the opinion of the investigator, confound interpretation of the study results
10. 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 the investigational agent (whichever is longer) prior to screening period
11. Women who are pregnant, or who are currently breastfeeding
12. Inability to cooperate or any condition that, in the opinion of the investigator, could increase the subject's risk by participating in the study

or confound the outcome of the study
13. Evidence of drug or alcohol abuse or dependence, in the opinion of the investigator
14. Known or suspected hereditary fructose intolerance.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-12-2021
Enrollment:	1
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Pegcetacoplan
Generic name:	Pegcetacoplan

Ethics review

Approved WMO

Date:	04-01-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	29-03-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-08-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-08-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-03-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-05-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-07-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-12-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-12-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-05-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	19-12-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-01-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-04-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-06-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-07-2024
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	CTIS2024-511544-36-00
EudraCT	EUCTR2020-002637-15-NL
CCMO	NL75809.091.20