An Open-Label Phase 2 Proof-of-Concept Study in Patients with C3 Glomerulopathy (C3G) or Immune-Complex Membranoproliferative Glomerulonephritis (IC-MPGN) Treated with ACH-0144471.

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See protocol P5:The primary objective of this study is to evaluate the efficacy of 12 months of oral ACH-0144471 in participants with C3G or ICMPGNbased on histologic scoring and proteinuriaThe secondary objectives of this study are: * To evaluate...

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

Summary

ID

NL-OMON50417

Source
ToetsingOnline

Brief title
N/A

Condition

- Immune disorders NEC
- Nephropathies

Synonym
C3 glomerulopathies, Dense Deposit Disease, disease of the complement system, kidney disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: C3 Glomerulopathy, Immune Complex Membranoproliferative Glomerulonephritis

Outcome measures

Primary outcome

See protocol P9:

Primary efficacy endpoints:

* Change from baseline in biopsy, based on a score incorporating changes in

both the activity index and C3 staining at the end of 12 months of treatment.

* Number and percent of participants with reduction in proteinuria relative to

baseline at the end of 12 months of treatment

Secondary outcome

See protocol P9:

Secondary efficacy endpoints:

* Number and proportion of participants with significant (*25%) increase in

eGFR relative to baseline at the end of 12 months of treatment

* Change and percent change from baseline in proteinuria and eGFR over 12

months of treatment period for all participants

* Change and percent change from baseline in eGFR over 12 months of treatment

for participants meeting eGFR inclusion criterion at study entry

* Descriptive analysis of slope of GFR over the treatment period of -4471

therapy

Study description

Background summary

See protocol P19-21:

1.2.1 Complement Factor D
Factor D is one of nine serine proteases in the complement system. It is a highly specific enzyme with only one known substrate, fB. Of all the complement proteins, it has the lowest abundance in serum with a concentration of approximately 2 *g/mL, and is the rate-limiting step of AP activation [2, 3]. It is a low molecular weight protein (24 kDa) that is primarily produced by adipocytes, but can also be produced and secreted by monocytes/macrophages and astrocytes in humans [2, 3]. Due to its small size, it is freely filtered at the glomerulus, and then taken up by the proximal tubule cell where it is catabolized with an estimated fractional catabolic rate of 60% per hour. It is this rapid catabolism that is responsible for maintaining low circulating fD levels. As a result, renal dysfunction is associated with elevated fD levels, which may lead to increased alternative pathway activity and inflammation [4, 5]. The biochemical, physiological, and functional features of fD make it an attractive target for pharmacological inhibition as this may prove useful in the treatment of a wide spectrum of complement-mediated diseases, including C3G and IC-MPGN.

11.2.2 C3 Glomerulopathy
C3 glomerulopathy (C3G) is an ultra-rare disease with an incidence rate of approximately 2 per million people worldwide [6, 7]. It is widely accepted that C3G is attributable to excessive alternative pathway(AP) activity [8]. Although the disease is typically diagnosed during early adulthood in a majority of patients, the manifestations of glomerular C3 deposition can be detected in childhood and thus, it may be clinically meaningful to treat patients as young as 12 years of age [7, 9, 10]. The clinical course of C3G is characterized by variable amounts of proteinuria, hematuria, hypertension, and decreased renal function, with approximately 30% to 50% of patients reaching end-stage renal disease (ESRD) within 10 years of diagnosis [7, 11, 12, 13]. The diagnosis is based on predominant deposition of C3 in the glomerulus on renal biopsy along with clinical evidence of AP hyperactivity. C3G can be further subdivided into two separate entities, dense deposit disease (DDD) and

C3 glomerulonephritis (C3GN), based on electron microscopic features of the renal pathology [8]. Although the two disorders have similar clinical features, DDD tends to present earlier in life than C3GN. However, both diseases can present in either childhood or adulthood [13].

Unfortunately, no specific therapy has proven effective for the treatment of C3G. Care is therefore largely non-specific and supportive. Given the lack of available therapeutic options, immunosuppressive and plasma infusion/exchange therapy are often attempted, as a subset of patients may benefit [13, 14]. Treatment is otherwise focused on management of hypertension, proteinuria and the manifestations of chronic kidney disease.

The overall prognosis of C3G is poor, with approximately 30% to 50% of patients progressing to ESRD within 10 years of diagnosis. Dialysis and renal transplantation are options available for patients who reach ESRD; however, disease recurrence is frequent after transplantation, occurring in more than 50% of patients. Only about 50% of patients have a functioning graft 5 years after transplantation, which is significantly lower than renal graft survival in other settings [13, 14, 15].

Studies in animal models have indicated that the pathophysiology of C3G strongly relates to an excessive AP activity at the level of the C3 convertase. Specifically, mouse factor H-deficient animals have evidence of uncontrolled alternative pathway activation, with low plasma levels of intact C3, high levels of C3 breakdown product and renal pathology consistent with C3G; yet, in mice deficient in both factor H (fH) and fD (knock-out mice), serum C3 levels were similar to wild-type and dense deposits were not present in the kidneys [16, 17]. These studies confirmed that removal of fD prevented the renal pathogenesis of C3G in the factor H-deficient mice.

Given that the pathophysiology of C3G derives from excessive C3 activation through the AP, treatment of the disease with an AP complement inhibitor is logical. Eculizumab, the only commercially available complement inhibitor, has been tested in patients with C3G, even though its mechanism of action (targeting the terminal complement pathway) would not be expected to affect C3 activation. Based on the published results of an open-label trial in 20 patients, the general consensus is that only a subset of patients appears to benefit from eculizumab therapy; however, identification of these patients prior to treatment remains a challenge [8, 13, 14, 18]. It has been suggested that response to eculizumab may be more likely in those patients with elevated soluble C5b-9 levels, indicative of excessive terminal pathway activity, although this hypothesis remains to be established [18].

A fD inhibitor like ACH-0144471, which inhibits directly at the level of the AP C3 convertase formation, provides a more targeted rationale for efficacy than existing complement inhibitors that target the terminal complement pathway. This hypothesis is supported by animal data in which the renal disease observed with factor H deficiency, which is similar to human C3G, was completely prevented in the setting of simultaneous fD or fB deficiency [16, 17]. In contrast C5 deficiency only ameliorated, but did not prevent, renal disease. Furthermore, C6 deficiency had no effect on the renal disease in fH deficient mice. Taken together, the data from the C5 and C6 deficient mice provide

evidence that the membrane attack complex itself plays little role in renal pathogenesis of C3G in the setting of fH deficiency, but that C5a production may be a factor contributing to disease [
13, 19].
1.2.3 Immune-Complex Membranoproliferative Glomerulonephritis (IC-MPGN)
Immune-complex membranoproliferative glomerulonephritis (IC-MPGN) is a renal disease which shares many clinical, pathologic, genetic, and laboratory features with C3G, and therefore can be considered a sister disease of C3G. In the majority of patients with IC-MPGN, an underlying disease or disorder (most commonly infections, autoimmune diseases or monoclonal gammopathies) are identified to which the renal disease is secondary. Of note, the most common infections associated with IC-MPGN are hepatitis B and C. Up to 40% of patients with IC-MPGN have no identifiable underlying etiology, and are considered to have primary IC-MPGN. Patients with primary IC-MPGN can have low C3 and normal C4 levels, similar to those observed in C3G, as well as many of the same genetic or acquired factors that are associated with abnormal alternative pathway activity. Although IC-MPGN pathology is at least in part attributable to overactivity of the classical pathway, evidence of C3 and/or C3 fragment staining on renal biopsy suggests alternative pathway-related pathophysiology [20]. IC-MPGN patients should therefore benefit from fD inhibition.

Study objective

See protocol P5:

The primary objective of this study is to evaluate the efficacy of 12 months of oral ACH-0144471 in participants with C3G or ICMPGN
based on histologic scoring and proteinuria

The secondary objectives of this study are:
* To evaluate the clinical effect of 12 months of oral ACH-0144471 in participants with C3G
or IC-MPGN based on significant improvement in slope of estimated glomerular filtration
rate (eGFR) relative to baseline over time
* To evaluate for improvement in eGFR following treatment with ACH-0144471
* Where available evaluate the change in measured (m) eGFR relative to baseline at the end of
12 months of treatment with ACH-0144471
* To evaluate the safety and tolerability of ACH-0144471 in participants with C3G or ICMPGN
by assessing serious adverse events (SAEs)

Study design

See protocol P23-24:

This is an open-label study in which all participants will receive active treatment with ACH-0144471 for approximately 24 months. The study will enroll approximately 20 participants with biopsy-confirmed C3G or IC-MPGN, 12 years of age or older, who have not undergone renal transplant. Participants who completed ACH471-201 are eligible to participate, as long as they do not meet any exclusion criteria.

Participants who did not participate in ACH471-201 must meet all inclusion and exclusion criteria to be eligible. In particular, they must have a biopsy-confirmed diagnosis of C3G or IC-MPGN. The initial diagnosis should have been made at least 3 months prior to dosing, unless otherwise approved by the sponsor. Participants must also have clinical evidence of ongoing disease (defined as proteinuria of *500 mg/day of protein in a 24-hour urine) that is attributable to C3G or IC-MPGN in the opinion of the Principal Investigator (PI). Participants who completed ACH471-201 may enroll in this study following a washout period of at least 30 days between the last dose of ACH-0144471 in study ACH471-201 and the renal biopsy (if collected during screening; Section 6.3) or the 24-hour urine collection during screening. These participants will not be required to re-establish their diagnosis of C3G or IC-MPGN, but must meet the other eligibility requirements described in Section 4.

For all participants, eligibility will be confirmed based on the results from the screening eligibility assessments. Once eligibility is confirmed, arrangements can be made for a renal biopsy (if necessary to confirm the diagnosis of C3G or IC-MPGN as described in Section 6.3.1, or to establish a baseline for participants who choose to participate in the renal biopsy sub-study as described in Section 6.3.2) and/or vaccinations. Biopsies will not be obtained from participants less than 18 years of age (unless a biopsy is determined to be clinically indicated by the treating provider), or from participants for whom a biopsy is contraindicated. The initial screening visit must occur no more than 75 days before the first dose date.

All participants should be vaccinated against Haemophilus influenzae (H. influenzae), Streptococcus pneumoniae (S. pneumoniae), and Neisseria meningitidis (N. meningitidis) as recommended by the Advisory Committee on Immunization Practices (ACIP) guidelines at least 2 weeks before the start of dosing with ACH*0144471, as described in Section 6.4, to minimize the risk of serious infection with an encapsulated organism, unless otherwise recommended by local vaccination guidelines, or precluded by licenses or availability. The PI may institute additional prophylactic measures, including the use of prophylactic antibiotics, if deemed appropriate by local clinical practice and/or guidelines for treatment with a complement inhibitor.

The starting dosage will be 100 mg of ACH-0144471 TID, for a total daily dose of 300 mg. After 2 weeks of treatment, dosing will be escalated to 200 mg TID (or 150 mg TID for participants less than 60 kg). For each participant, the medical monitor will consult with the investigator before making the decision to dose escalate. Upon treatment discontinuation, regardless of the timing or reasons for discontinuation, a 6-day taper period is required unless the PI determines this taper period poses a risk to the participant. The taper period is in place to prevent the theoretical risk of marked increase or rebound in

complement activity, as described in Section 5.1.1.
A sub-study is being conducted to evaluate the effects of ACH*0144471 on renal pathology (see Section 6.3.2); participation in this study is not required. For participants in the renal biopsy sub-study, biopsies will be obtained prior to dosing and after approximately 28 and 104 weeks of dosing. Only one biopsy will be obtained prior to dosing; If for any reason, any additional renal biopsies are performed (e.g., for a clinical indication), then every effort will be made to make these biopsy samples and results available to the central pathology laboratory for evaluation.
Patient-reported outcome (PRO) questionnaires will be administered to participants at various time points as specified in the Schedule of Assessments (Appendix 1), to assess participants* health-related quality of life (HRQOL), fatigue, and kidney-related fears and worries (e.g. kidney failure, dialysis, kidney transplant), and to determine health states value, over the course of treatment with ACH-0144471.

Intervention

See protocol P36-37:

ACH-0144471 tablets will be administered at a starting dosage of 100 mg TID. Study drug administration will then continue for the remainder of the 24-month Treatment Period. When dosing is to be discontinued, the dose will be tapered over approximately six days (Taper Period) to minimize the potential adverse effects of a rapid surge in complement activity following drug withdrawal.

For the starting dose, participants will take one 100-mg ACH-0144471 tablet three times daily (TID): a dose in the morning, a second dose 8 hours later, and a third dose 8 hours after the second dose. Doses should be taken at approximately the same time each day and as close as possible to 8 hours apart. All doses should be taken approximately 15 to 30 minutes after completion of a meal. Water intake is not restricted. If a dose is missed, it should be taken within 4 hours of the originally scheduled time. After 4 hours, the missed dose should be skipped. In either case, the next dose should be taken according to the original dosing schedule.

Dose Adjustment
After 2 weeks of treatment, dosing will be escalated to 200 mg TID (or 150 mg TID for participants less than 60 kg) unless the participant has not tolerated treatment. While the intent is to maintain a steady dose for the duration of the study, dose adjustments are permitted for participant safety or in order to create the best opportunity for each participant to have a therapeutic benefit. Dosing may be adjusted by the MM (or designee) in consultation with the PI, within the parameters provided below and based on review of available safety, PK, and PD results.
Dose increases should be such that the new total daily dose is no more than 2×

the prior total daily dose.

Study burden and risks

See protocol P19:
Benefit:
ACH-0144471, a small molecule, orally administered, factor D (fD) inhibitor, is in development by Achillion Pharmaceuticals, Inc. (*Achillion*, or the sponsor) for the treatment of complement-related diseases, such as paroxysmal nocturnal hemoglobinuria (PNH) and C3 glomerulopathy (C3G). Factor D is a serine protease that catalyzes the cleavage of factor B, a rate-limiting step in the alternative pathway (AP) of complement. By inhibiting fD, ACH-0144471 potently and specifically inhibits AP activity.
Because C3G is a disease of AP hyperactivity, ACH-0144471 represents an ideal therapeutic approach to C3G, as it has the potential to reverse the underlying pathophysiology of the disease. Primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN), which shares many clinical, pathologic, genetic, and laboratory features with C3G and in which complement also likely plays a key role, may also be an attractive therapeutic target.

See protocol P28-29:
Risks:
Risk of Infection:
Since one of the primary functions of the complement system is to fight infections, pharmacologic inhibition of the complement system could theoretically result in an increased rate or severity of infections. However, high doses of C1 esterase inhibitor in transplant patients with rejection did not show a signal for infection [36]. Thus, it remains unclear as to whether fD inhibition would increase risk for infection.
In vitro work was done to understand potential infection risk, especially meningococcal infection risk that is associated with AP inhibition. As summarized in Sections 4.1.2 and 6.5.1 of the Investigator's Brochure [1], ACH-0144471 showed minimal inhibition of protective bactericidal and opsonophagocytic activities in studies that included several strains of the clinically important pathogen N. meningitidis and blood samples from immunized individuals, suggesting that vaccination should provide protection from meningococcal infections in participants receiving ACH-0144471.
Nonetheless, this study takes steps to minimize the risk of serious infection. Participants should be vaccinated according to applicable national and/or local guidelines or local clinical practice for N. meningitidis, H. influenza, and S. pneumonia (see Section 6.4), and antibiotic prophylaxis is permitted if deemed appropriate by local clinical practice and/or guidelines, as described in Section 6.5. Achillion will also create and distribute a wallet card for outpatient studies with warning signs and symptoms of serious infection, and appropriate steps of action for all participants. Finally, a fever management plan has been incorporated into the study protocol (see Appendix 2).

Hepatic Injury:
Hepatobiliary cholestasis has been observed in dog toxicology studies at exposures higher than those intended for clinical use, and higher than those planned for this study. Based on clinical observations, the cholestasis is reversible and can be monitored with hepatic safety biomarkers.
Elevations of transaminases have occurred clinically with ACH-0144471. Grade 3 or Grade 4 liver enzyme elevations occurred in 2 active phase 1 study participants receiving higher doses of ACH-0144471 (500 mg twice daily [BID] and 800 mg BID), although these elevations occurred after dosing was completed (3 days and 7 days after last dose). One PNH participant had elevated transaminases associated with breakthrough hemolysis and discontinued ACH-0144471. All abnormal transaminase findings were transient, were not associated with evidence of hepatic decompensation, and resolved within a short time period. Transaminases will be monitored in this study.
Stopping criteria have been included ensuring prompt discontinuation of any participant with evidence of unexplained liver injury. Finally, participants with evidence of active hepatic or hepatobiliary disease will be excluded.

Contacts

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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

Each participant must meet all of the following criteria to be enrolled in this study:
1. Must have completed the C3G Proof of Mechanism (POM) study (ACH471-201) (participation in the long-term follow-up portion of ACH471-201 is not required),
OR
Must meet all the following criteria:
a. Must have biopsy-confirmed primary C3G or IC-MPGN
b. Must have clinical evidence of ongoing disease based on significant proteinuria (defined as *500 mg/day of protein in a 24-hour urine) attributable to C3G disease or IC-MPGN in the opinion of the PI, and present prior to study entry and confirmed during Screening.
c. If a pre-treatment biopsy is obtained, or if a historical biopsy is available for review, it must have no more than 50% global fibrosis and no more than 50% of glomeruli with cellular crescents
d. Must be 12 years or age or older and capable of swallowing tablets
2. If on corticosteroids, anti-hypertensive medications, anti-proteinuric medications (e.g., ACE inhibitors or angiotensin receptor blockers [ARBs]), or mycophenolate mofetil (MMF), must be on a stable dose for at least 2 weeks prior to screening
3. Female participants of childbearing potential must agree to use an acceptable method of contraception (as defined in Section 5.5.5) from the date of signing the informed consent to the first day of dosing (Day 1), and must agree to use a highly effective form of contraception (as defined in Section 5.5.5) from the first day of dosing to 30 days after their last dose of study drug. Female participants of childbearing potential must also have a negative serum pregnancy test during Screening and negative urine pregnancy test on Day 1. Female participants of non-childbearing potential need not employ a method of contraception.
4. Non-sterile male participants must agree to use a highly effective form of contraception (as defined in Section 5.5.5) with their partner(s) of childbearing potential from the first day of dosing to 90 days after their last dose of study drug. Male participants who are surgically sterile need not employ additional contraception. Male participants must agree not to donate sperm while enrolled in this study and for up to 90 days after their last dose

of study drug.
5. Adult participants must be capable of providing written informed consent and adolescent participants must be capable of providing written assent. All participants must be willing and able to comply with the requirements and restrictions listed in the consent form and with all procedures in the protocol, including, the visit schedule, the treatment plan, the schedule for laboratory testing, and other study procedures
6. Must be up-to-date on routine vaccinations, or willing to be brought up-to-date, based on local guidelines
7. Must have access to emergency medical care

Exclusion criteria

Participants who meet any of the following criteria will be excluded from the study.
1. Have a history of a major organ transplant (e.g., heart, lung, kidney, liver) or hematopoietic stem cell/marrow transplant
2. Have a history or presence of any clinically relevant co-morbidities that would make the participant inappropriate for the study (for example, a comorbidity which is likely to result in deterioration of the participant*s condition, affect the participant*s safety during the study, or confound the results of the study), in the opinion of the PI
3. Have an estimated GFR <30 mL/min/1.73 m2 at the time of screening or at any time over the preceding four weeks
4. Is a renal transplant recipient or receiving renal replacement therapy
5. Have other renal diseases that would interfere with interpretation of the study
6. Have evidence of monoclonal gammopathy of unclear significance (MGUS), infections, malignancy, autoimmune diseases, or other conditions to which C3G or IC-MPGN is secondary
7. Have been diagnosed with or show evidence of hepatobiliary cholestasis
8. Females who are pregnant, nursing, or planning to become pregnant during the study or within 90 days of ACH-0144471 administration or participants with a female partner who is pregnant, nursing, or planning to become pregnant during the study or within 90 days of ACH-0144471 administration
9. Have a history of febrile illness, a body temperature >38°C, or other evidence of a clinically significant active infection, within 14 days prior to ACH-0144471 administration
10. Have evidence of human immunodeficiency virus (HIV), hepatitis B infection, or active hepatitis C infection at Screening
11. Have a history of meningococcal infection within the prior year
12. Have a history of hypersensitivity reactions to commonly used antibacterial agents, including beta-lactams, penicillin, aminopenicillins, fluoroquinolones, cephalosporins, and carbapenems, which, in the opinion of the investigator and/or an appropriately qualified immunology or infectious disease expert,

would make it difficult to properly provide either empiric antibiotic therapy or treat an active infection.
13. Have participated in a clinical study in which an investigational drug was given within 30 days, or within 5 half-lives of the investigational drug, whichever is longer, prior to the first dose of ACH-0144471
14. Have received eculizumab at any dose or interval within the past 50 days prior to the first dose of ACH-0144471
15. Have received tacrolimus or cyclosporine within 2 weeks of the first dose of ACH-0144471
16. Have a 12-lead ECG with a QTcF >450 msec for males or >470 msec for females, or have ECG findings which, in the opinion of the PI, could put the participant at undue risk
17. Have received any drug known to prolong the QTc interval within 2 weeks of the first dose of ACH-0144471 and which, in the opinion of the PI, could put the participant at undue risk
18. Have any of the following laboratory abnormalities at screening:
* Alanine transaminase (ALT) > upper limit of normal (ULN)
* Aspartate aminotransferase (AST) > ULN
* Absolute neutrophil counts (ANC) <1,000/*L
* Total bilirubin >1.5× ULN
* Indirect bilirubin > ULN
* Any laboratory abnormality that, in the opinion of the PI, would make the participant inappropriate for the study
19. Are unwilling or unable to comply with the study protocol for any reason

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-02-2019
Enrollment:	3

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ACH-0144471
Generic name:	Danicopan

Ethics review

Approved WMO Date:	18-07-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-01-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-02-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-05-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-06-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-06-2019

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-07-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-09-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-10-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-03-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-05-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-06-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-07-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-08-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-10-2020

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
EudraCT	EUCTR2017-002674-39-NL
ClinicalTrials.gov	NCT03459443
CCMO	NL64457.091.18