Phase 3 Randomized, Placebo-Controlled Study to Assess Safety, Tolerability, and Efficacy of Garetosmab in Patients with Fibrodysplasia Ossificans Progressiva

Published: 14-09-2022
Last updated: 14-09-2024

This study has been transitioned to CTIS with ID 2023-508350-26-00 check the CTIS register for the current data. Primary ObjectiveThe primary efficacy objective of the study is to assess the effect of garetosmab (10 mg/kg) versus placebo on the...

Ethical review	Approved WMO
Status	Pending
Health condition type	Bone disorders (excl congenital and fractures)
Study type	Interventional

Summary

ID

NL-OMON53784

Source
ToetsingOnline

Brief title
R2477-FOP-2175 (ICON 0456/0477)

Condition

- Bone disorders (excl congenital and fractures)

Synonym
uiterst zeldzame genetische bindweefselaandoening, verbening

Research involving
Human

Sponsors and support

Primary sponsor: Regeneron Pharmaceuticals Inc.

Source(s) of monetary or material Support: The study sponsor as listed in B6/7.

Intervention

Keyword: Bone disease, Firbodysplasia Ossificans Progressiva

Outcome measures

Primary outcome

Primary Efficacy Endpoint:

The primary efficacy endpoint is the number of new HO lesions adjudicated as

positive based on CT at week 56.

Primary Safety Endpoint:

The primary safety endpoint is the incidence and severity of treatment emergent

adverse

events of special interest (AESIs) from baseline to week 56.

Secondary outcome

Secondary study parameters/outcome of the study (if applicable) (in Dutch):

Key Secondary Endpoint:

The key secondary endpoint is the number of clinician-assessed flare ups

through week 56.

Secondary Efficacy Endpoints

The secondary efficacy endpoints are:

• The number of clinician-assessed flare-ups through week 28

• Occurrence of clinician-assessed flare-ups through weeks 28 and 56 (Yes/No)

• The number of patient-reported flare-ups through weeks 28 and 56

• Occurrence of patient-reported flare-ups through weeks 28 and 56 (Yes/No)

• Occurrence of new HO lesions adjudicated as positive based on CT at week 28

and 56 (Yes/No)

• Total volume of new HO lesions adjudicated as positive based on CT at weeks 28 and 56

• Number of new HO lesions adjudicated as positive based on CT at week 28

• Change from baseline in joint function assessment by physician to week 28 and week 56 by the CAJIS

• Change from baseline in pulmonary function as assessed by spirometry at week 28 and week 56

• Change from baseline in disease severity to week 28 and week 56 by the PGIS

• Change since the start of the study in disease severity to week 28 and week 56 by the PGIC

• Change since the start of the study in disease severity to week 28 and week 56 by the CGIC

For patients continuing extended treatment, additional other secondary efficacy endpoints are:

• Number of new HO lesions adjudicated as positive based on CT at week 84

• Occurrence of new HO lesions adjudicated as positive based on CT at week 84 (Yes/No)

• Total volume of new HO lesions adjudicated as positive based on CT at week 84

• The number of clinician-assessed flare-ups through week 84

• Occurrence of clinician-assessed flare-ups through week 84 (Yes/No)

Note: To ensure consistency of assessments, it is advised that the same clinician

performs the clinician-assessed FOP flare-ups and CAJIS evaluations, at all

visits for the mentioned assessments for a given patient, whenever possible.

Study description

Background summary

Fibrodysplasia ossificans progressiva (FOP) is an ultra-rare, severely disabling, congenital genetic disease characterized by progressive multi-focal heterotopic ossification (HO) of skeletal muscle, ligaments, tendons, and fascia. Heterotopic ossification is the abnormal growth of bone in non skeletal tissues. FOP is estimated to occur in approximately 1 in 0.63 to 1.86 million individuals based on reports of diagnosed cases (Liljesthro*m, 2020). There are approximately 800 confirmed cases of FOP globally. No ethnic, racial, gender, or geographic predisposition has been reported. Palovarotene, a retinoic acid receptor gamma (RAR*) selective agonist, is approved only in Canada for the reduction of HO in adults and children >8 years for females and >10 years for males with FOP. Fibrodysplasia ossificans progressiva is caused by dominant missense mutations in the intracellular domain of activin receptor type 1A (ACVR1, also known as ALK2), a bone morphogenetic protein (BMP) type I receptor which is expressed in many tissues of the body, including skeletal muscle and cartilage (Huning, 2014). Although FOP is caused by a variety of such mutations, the great majority of FOP patients carry the point mutation, c.617G>A; p.R206H, which alters arginine (R) 206 to a histidine (H) (Huning, 2014). A significant breakthrough in the understanding of FOP occurred in 2015 when it was demonstrated that FOP-causing mutations of ACVR1 render this receptor responsive to activin A and initiate signaling through the SMAD 1/5/8 pathway, akin to that obtained from osteogenic BMPs (Hatsell, 2015) (Hino, 2015). In contrast, when activin A engages wildtype ACVR1 receptors, it forms a non-signaling complex, and as a result activin A antagonizes BMP pathway signaling mediated by wild-type ACVR1(Aykul, 2020) (Hatsell, 2015). The ACVR1[R206H] variant was subsequently expressed in a conditional inducible mouse model of FOP. These mice developed progressive HO at anatomic locations similar to those seen in patients with FOP, as detected by 18F-NaF PET/CT which labeled active HO and volumetric CT (Hatsell, 2015) (Upadhyay, 2017). Inhibition of activin A with the neutralizing anti-activin A antibody garetosmab blocked the development of new HO lesions and also resulted in stasis or partial resorption of existing (but nascent) HO lesions. These results suggested a fundamental role for activin A in the initiation and progression of HO, and that an anti-activin A antibody might provide beneficial clinical impact on HO in patients with FOP (Upadhyay, 2017). Recently, experiments in the ACVR1[R206H] FOP mice have been extended to another FOP-causing ACVR1 variant, R258G. This ACVR1[R258G] mouse model developed HO

much like the ACVR1[R206H] mouse model, and HO was again inhibited by garetosmab. Hence, inhibition of activin A is a promising therapeutic approach for halting HO in FOP, whether it arises as a result of the most common FOP-causing variant of ACVR1, ACVR1[R206H], or any of the other FOP-causing variants of ACVR1 reported to date. Garetosmab is a fully human monoclonal antibody (mAb) that selectively binds activin A, AB, and AC, blocking their ability to interact with their corresponding type I receptors and hence block signaling. Garetosmab has been studied in 2 completed trials in healthy adult subjects. R2477-HV-1525 was a first in human (FIH), double-blind, placebo-controlled, single-ascending dose study in women of non-childbearing potential (30 healthy subjects were exposed). R2477-1033-HV-1621 was a randomized, double-blind, placebo-controlled, ascending-dose study to assess the safety, tolerability, and pharmacodynamic (PD) effects of garetosmab alone and in combination with trevogrumab (an anti-myostatin mAb) in healthy postmenopausal women and healthy adult men (56 healthy subjects were exposed to garetosmab alone or in combination with trevogrumab). The results of the studies in healthy subjects showed that overall, garetosmab was well tolerated with no significant safety findings observed. The clinical benefit of garetosmab for the treatment of FOP was demonstrated in the phase 2, double-blind, placebo-controlled, 28-week treatment study (LUMINA-1), followed by 2 open label periods. While garetosmab did not have a significant effect on the planned primary endpoint, total lesion activity (measuring a reduction in the size and activity of pre-existing HO lesions), there was a striking reduction in the number of new HO lesions as assessed by both 18F NaF PET and CT in adult patients with FOP. These substantive and clinically meaningful reductions were largely demonstrated by significant decreases in the incidence and volume of new lesions after 28 weeks of treatment. Moreover, garetosmab reduced the incidence of patient- and investigator reported flare-up events. Results from the open-label period showed sustained efficacy with long-term treatment through week 76. From a safety perspective, the majority of treatment-emergent adverse events (TEAEs) were mild to moderate in severity. Infusion reactions were balanced between treatment groups with no serious or severe events. Notable imbalances in TEAEs included epistaxis, acne, madarosis (thinning of the eyelashes or eyebrows), and a composite of skin infections including abscesses, carbuncle, folliculitis, and furuncle. Additional background information on the study drug and development program can be found in the IB.

Study objective

This study has been transitioned to CTIS with ID 2023-508350-26-00 check the CTIS register for the current data.

Primary Objective
The primary efficacy objective of the study is to assess the effect of garetosmab (10 mg/kg) versus placebo on the formation of new HO lesions from baseline to week 56, as determined by low dose CT.

The primary safety objective of the study is to assess the safety and tolerability of garetosmab (10 mg/kg, 3 mg/kg) versus placebo from baseline to week 56.

Secondary Objectives
Key Secondary Objectives
The key secondary objectives of the study are:
• To assess the effect of garetosmab 10 mg/kg versus placebo on the number per patient of clinician assessed flare-up episodes to week 56
• To assess the effect of garetosmab (3 mg/kg) versus placebo on the formation of new HO lesions from baseline to week 56 as determined by CT
• To assess the effect of garetosmab (3 mg/kg) versus placebo on the number per patient of clinician assessed flare-up episodes to week 56
Secondary Objectives
All other secondary objectives will compare the 10 mg/kg dose group to the placebo group and the 3 mg/kg dose group to the placebo group at week 28 and week 56 unless otherwise specified.
Other secondary objectives of the study are:
• To assess the effect of garetosmab versus placebo on the occurrence of clinician-assessed flare-up episodes
• To assess the effect of garetosmab versus placebo on the number per patient of clinician assessed flare-up episodes to week 28
• To assess the effect of garetosmab versus placebo on the occurrence of patient reported flare up episodes
• To assess the effect of garetosmab versus placebo on the number per patient of patient reported flare-up episodes
• To assess the effect of garetosmab versus placebo in the proportion of patients with new HO lesions as determined by CT
• To assess the effect of garetosmab versus placebo on volume of new HO lesions as determined by CT
• To assess the effect of garetosmab versus placebo on the number of new HO lesions per patient from baseline to week 28 as determined by CT
• To characterize the concentrations of total activin A
• To evaluate concentrations of garetosmab
• To assess the immunogenicity of garetosmab
• To assess the effect of garetosmab versus placebo in pulmonary function assessed by pulmonary function tests
• To assess clinical outcomes (ie, joint function [Cumulative Analog Joint Involvement Scale (CAJIS)]) at baseline and over time after the first dose of garetosmab versus placebo
• To assess the effect of garetosmab versus placebo on patient's disease severity assessed by the Patient Global Impression of Severity (PGIS)
• To assess the effect of garetosmab versus placebo on patient's change in disease assessed by the Patient's Global Impression of Change (PGIC)
• To assess the effect of garetosmab versus placebo on clinician's change in disease assessed by the Clinician's Global Impression of Change (CGIC)
• To assess the safety and efficacy of garetosmab beyond 12 months.

Exploratory Objectives
The exploratory objectives of the study are:
• To assess the effect of garetosmab versus placebo in the number of pre-existing HO lesions that disappear as assessed by CT compared with baseline
• To assess, including but not limited to, biochemical markers of bone formation, hypertrophic cartilage, inflammation, and activin A related ligands at baseline and over time after the first dose of garetosmab
• To assess platelet function in patients treated with garetosmab via flow cytometry
• To explore genetic associations with FOP or treatment response in an optional genetics sub-study
• To assess the effect of garetosmab on lung volume
• To assess the EuroQol 5 dimensions questionnaire with a 3-level scale (EQ-5D-3L) at baseline and over time after the first dose of garetosmab versus placebo
• To assess quality of life at baseline (via Short-Form 36 [SF-36]) and over time after the first dose of garetosmab versus placebo
• To explore the relationship of garetosmab concentration and the efficacy and safety response
• To assess the effect of garetosmab on the duration of flare and severity level of flare

Study design

R2477-FOP-2175 is a phase 3, randomized, multi-center, multinational, parallel-group, placebo-controlled study to assess the efficacy of garetosmab on the reduction of heterotopic bone formation, and its safety, tolerability, and PK in FOP patients with active disease caused by any FOP-causing variant of ACVR1. Approximately 66 patients will be enrolled 1:1:1 into the 3 parallel arms of the study. The study consists of 4 periods and a Follow-up Safety Visit.

Screening Period: 4 weeks in duration (from study day -28 to day -1 [visit 1]). All patients will undergo an informed consent process and screening procedures. Screening procedures may be conducted over multiple days.

Double-Blind Treatment Period (DBTP): 56 weeks in duration (from study day 1 [visit 2] to week 56 [visit 17]). All patients will be randomized to doubleblind treatment with garetosmab 10 mg/kg, garetosmab 3 mg/kg, or placebo.

Extended Treatment Period (ETP): 28+ weeks in duration (study week 56+ [visit 17+]) for those who choose to continue double-blind treatment. Patients who complete the DBTP and elect to extend double-blind treatment continue until the last global patient completes week 84.

Observation Period: 28+ weeks in duration (study week 56+ [visit 17+]) for those who choose to discontinue from double-blind treatment. Patients who

complete the DBTP and elect to go unblinded and stop treatment will be followed to assess survival and any pertinent safety events (ie, severe bleeding) since the last contact. The Observation Period will continue until the last global patient completes their last study visit. Patients will not receive treatment and may participate in other studies.

Follow-Up Safety Visit: 30 weeks from the last dose administered (study week 84+ [visit 24+]) for all patients who receive treatment, except for patients who are unblinded that were treated with placebo (placebo-treated patients unblinded at week 56 [visit 17] do not participate in the Follow-Up Safety Visit). Consists of a safety follow-up visit 30 weeks after the last study drug administration.

Efficacy assessments will include whole body CT for HO lesions, assessment of flare-ups, CAJIS, pulmonary function tests, change in disease severity, and quality of life (EuroQol 5 dimensions questionnaire with a 3-level scale [EQ5D-3L] and Short-Form 36 [SF-36]).
Safety assessment will include adverse events (AEs), vital signs, physical examination, Electrocardiograms (ECGs), serum and urine laboratory testing, ear nose, and throat (ENT) consultation, coagulation parameters, platelet flow cytometry, and menstrual cycle history.
Patients who participated in the phase 2, R2477-FOP-1623 study (LUMINA-1) can enroll if they meet the inclusion criteria and do not meet the exclusion criteria.

Intervention

Study Drug: Garetosmab is supplied as a liquid drug product and will be administered intravenous (IV) in this study.

Dose/Route/Schedule: Patients will receive either garetosmab IV (10 mg/kg) every 4 weeks (Q4W), garetosmab IV (3 mg/kg) Q4W, or matching placebo Q4W.

Placebo Route/Schedule: Placebo to match garetosmab is supplied as a liquid solution without the monoclonal antibody (or the protein).

Study burden and risks

Potential benefit of this study and a summary of the safety and efficacy data from LUMINA-1 are described previously in Section 1 and the IB. Because patients with FOP suffer from a severe, debilitating, and ultimately fatal genetic disease, it is proposed that the potential benefit of garetosmab in reducing HO activity outweighs any potential risks previously outlined.
Five deaths were reported in the open-label period of LUMINA-1. The sponsor investigated these events extensively, and the majority of these deaths appear consistent with common causes of death in patients with FOP, and with the life

expectancy in patients with FOP of similar age and disease severity as measured by the clinical staging of FOP developed by Pignolo et al (Pignolo, 2018).
Thus, a clear relationship to treatment was not identified. However, as these deaths occurred in the absence of a placebo group in the open-label period of the LUMINA-1 study, the possibility of an association cannot be excluded.
Therefore, this phase 3 study has been designed to further evaluate the benefit-risk profile of garetosmab in adult patients with FOP. This study will include an extended 1-year placebo arm which will allow for controlled assessment of safety, while the addition of inclusion/exclusion criteria will restrict the population to those with lower likelihood of morbidity and mortality due to the disease itself (ie, lower CAJIS and less disability), and allow the sponsor to better determine the relationship of study drug to adverse events. In addition, the ETP will allow the sponsor to understand better the long-term safety profile of garetosmab.
Specific safety considerations and risk mitigation strategies for the study are described in the sections below. These measures will be described in the informed consent form (ICF).
A risk-benefit statement with respect to the overall development program is provided in the IB.

Contacts

Public
Regeneron Pharmaceuticals Inc.

Old Saw Mill River Road 777
Tarrytown NY 10591
US
Scientific
Regeneron Pharmaceuticals Inc.

Old Saw Mill River Road 777
Tarrytown NY 10591
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Male or female 18 years or older at screening
2. Clinical diagnosis of Fibrodysplasia Ossificans Progressiva (FOP) [(based on findings of congenital malformation of the great toes, episodic soft tissue swelling, and/or progressive Heterotopic Ossification (HO)]
3. Confirmation of FOP diagnosis with documentation of Type I activin A receptor (ACVR1) FOP causing mutation
4. FOP disease activity within 1 year of screening visit. FOP disease activity is defined as pain, swelling, stiffness, or other signs and symptoms associated with FOP flare-ups; or worsening of joint function, or radiographic progression of HO lesions (increase in size or number of HO lesions) with/without being associated with flare-up episodes
5. Willing and able to undergo CT imaging procedures and other procedures as defined in the protocol
6. Willing and able to comply with clinic visits and study-related procedures
7. Provide informed consent signed by study patient or legally acceptable representative
8. Able to understand study-related questionnaires

Exclusion criteria

A patient who meets any of the following criteria will be excluded from the study:
1. CAJIS score at screening >19
2. Patient has significant concomitant illness or history of significant illness such as but not limited to cardiac, renal, rheumatologic, neurologic, psychiatric, endocrine, metabolic, or lymphatic disease, that in the opinion of the study investigator might confound the results of the study or pose additional risk to the patient by their participation in the study
3. Previous history or diagnosis of cancer (exceptions: localized basal/squamous cell cancer
that has been successfully excised; in situ cervical cancer)
4. Severely impaired renal function defined as estimated glomerular filtration rate <30 mL/min/1.73 m^2 calculated by the Modification of Diet in Renal Disease equation
(1 retest is allowed)

5. Uncontrolled diabetes defined as hemoglobin A1C (HbA1c) >9% at screening (1 retest is allowed)
6. History of poorly controlled hypertension, as defined by:
a. Systolic blood pressure >=180 mm Hg or diastolic blood pressure >=110 mm Hg at the screening visit
b. Systolic blood pressure of 160 mm Hg to 179 mm Hg or diastolic blood pressure of 100 mm Hg to 109 mm Hg at the screening visit, AND a history of end-organ damage (including history of left-ventricular hypertrophy, heart failure, angina, myocardial infarction, stroke, transient ischemic attack, peripheral arterial disease, end-stage renal disease, and moderate-to-advanced retinopathy [hemorrhages or exudates, papilledema])
7. Known history of cerebral vascular malformation
8. Cardiovascular conditions such as New York Heart Association class III or IV heart failure, cardiomyopathy, intermittent claudication, myocardial infarction, or acute coronary syndrome within 6 months prior to screening; symptomatic ventricular cardiac arrhythmia (Note: sinus dysrhythmia, asymptomatic block or well-controlled atrial fibrillation with normal resting ventricular rate are not exclusion criteria.)
9. History of severe anemia requiring transfusion
10. Patients who are on concomitant antiplatelet therapy (eg, clopidogrel), anticoagulants (eg, warfarin, heparin, factor Xa inhibitor, or thrombin inhibitors) in the last 30 days or within 5 half-lives of the therapy, whichever is longer. Low-dose acetylsalicylic acid (aspirin <=100 mg or <=150 mg/day, based on local practice) is acceptable.
(NOTE: low doses of heparin for flushing of catheters will be permitted.)
11. Patients with a history of severe, non-traumatic bleeding requiring transfusion or hospitalization for hemodynamic compromise (eg, severe nose bleeds requiring hospitalization, nasal packing or cauterization, menstrual bleeding that is prolonged/heavy)
12. Patients with a known pre-existing medical history of a bleeding diathesis (eg, hemophilia A, von Willebrand*s Factor deficiency, platelet count <=20×10^9/L)
13. Ongoing significant viral illness or pneumonia within 2 weeks of screening
14. History of severe respiratory compromise requiring oxygen, respiratory support (eg, bilevel positive airway pressure [biPAP] or continuous positive airway pressure [CPAP]), or a history of aspiration pneumonia requiring hospitalization
15. Known history of recent epididymitis (within 6 months of screening) or sexually transmitted diseases affecting urogenital organs
16. Prior use in the past year and concomitant use of bisphosphonates
17. Concurrent participation in another interventional clinical study or a non-interventional study with radiographic measures or invasive procedures (eg, collection of blood or tissue samples). Participation in the FOP Connection Registry or other studies in which patients complete study questionnaires is allowed
18. Treatment with another investigational drug, denosumab, imatinib or isotretinoin in the last 30 days or within 5 half-lives of the investigational

drug, whichever is longer
19. Known hypersensitivity to garetosmab or any of its excipients
20. Positive serum human chorionic gonadotropin (hCG)/urine pregnancy test at the screening/baseline visit
21. Members of the clinical site study team and/or his/her immediate family, unless prior approval granted by the sponsor
22. Patients who are committed to an institution by virtue of an order issued either by the judicial or the administrative authorities
23. Has received a COVID-19 vaccination (initial series or booster) within 1 week of planned start of study medication or for which the planned COVID-19 vaccinations would not be completed 1 week prior to start of study drug
24. Pregnant or breastfeeding women
25. Women of childbearing potential (WOCBP)* who are unwilling to practice highly effective contraception or undergo pregnancy tests prior to the initial dose, during the study, and for at least 30 weeks after the last dose. Highly effective contraceptive measures include:
a. stable use of combined (estrogen- and progestogen-containing) hormonal contraception (oral) associated with inhibition of ovulation initiated 2 or more menstrual cycles prior to screening,
b. intrauterine device (IUD); intrauterine hormone-releasing system (IUS),
c. bilateral tubal ligation/occlusion,
d. vasectomized partner (provided that the male vasectomized partner is the sole sexual partner of the WOCBP study patient and that the vasectomized partner has obtained medical assessment of surgical success for the procedure),
e. and/or sexual abstinence *,*

Pregnancy testing and contraception are required for WOCBP.
Pregnancy testing and contraception are not required for women who are post-menopausal or permanently sterile.

*WOCBP are defined as women who are fertile following menarche until becoming postmenopausal, unless permanently sterile. Permanent sterilization methods include hysterectomy, bilateral salpingectomy, and bilateral oophorectomy. A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high FSH level in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy. However, in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient to determine the occurrence of a postmenopausal state. The above definitions are according to the Clinical Trial Facilitation Group (CTFG) guidance.
* Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study drugs. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the patient.
* Periodic abstinence (calendar, symptothermal, post-ovulation methods), withdrawal (coitus interruptus), spermicides only, and lactational amenorrhea

method (LAM) are not acceptable methods of contraception. Female condom and male condom should not be used together.

26. Male patients with WOCBP partners* who are not willing to use condoms with WOCBP partners to prevent potential fetal exposure, during the study, and for 30 weeks after the last dose. Sperm donation is prohibited during the study and for 30 weeks after the last dose of study drug.

*Male patients with WOCBP partners will be asked to inform and ensure their female partners to use highly effective contraception measures * to prevent pregnancy.
* Vasectomy with medical assessment of surgical success and sexual abstinence * are considered highly effective contraception measures.
* Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study drugs. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the pat

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:	Pending
Start date (anticipated):	09-12-2022
Enrollment:	6
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Garetosmab
Generic name:	Garetosmab

Ethics review

Approved WMO Date:	14-09-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-07-2023
Application type:	First submission
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	17-08-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Approved WMO Date:	25-08-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-10-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-03-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	CTIS2023-508350-26-00
EudraCT	EUCTR2022-000880-40-NL
ClinicalTrials.gov	NCT04577820
CCMO	NL81750.018.22