REducing Lung congestIon symptoms using the v-wavE shunt in adVancEd Heart Failure

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The objective of the RELIEVE-HF study is to provide reasonable assurance of safety and effectiveness of the V-Wave Interatrial Shunt System by improving meaningful clinical outcomes in patients with NYHA functional class II, class III or ambulatory…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON52896

Source
ToetsingOnline

Brief title
RELIEVE-HF

Condition

- Heart failures

Synonym
Cardiomyopathy, Heart Failure

Research involving
Human

Sponsors and support

Primary sponsor: V-Wave Ltd.- Olivia Mishall
Source(s) of monetary or material Support: Industrie: V-Wave;Ltd.

Intervention

Keyword: Heart Failure, Interatrial Shunt, Lung Congestion

Outcome measures

Primary outcome

Primary Safety Endpoint:

The percentage of Treatment Group patients experiencing device-related Major Adverse Cardiovascular and Neurological Events (MACNE) during the first 30-days after randomization, compared to a pre-specified Performance Goal.

Primary Effectiveness Endpoint:

Comparison between Treatment and Control groups of the hierarchical composite ranking of all-cause death, cardiac transplantation or left ventricular assist device (LVAD) implantation, recurrent HF hospitalizations (including Emergency Room HF Visits with duration >=6 hours), recurrent worsening HF events treated as an outpatient (including ER visits < 6 hours), and change in KCCQ overall score. The analysis is based on the method of Finkelstein and Schoenfeld.

Secondary outcome

Hierarchically Tested Secondary Effectiveness Endpoints:

The following secondary endpoints will be tested hierarchically. The order of hierarchical endpoints testing will be specified in the Statistical Analysis

Plan.

- KCCQ changes from Baseline to 12 months
- Heart failure hospitalizations adjusted for all cause mortality
- Time to all-cause death, LVAD/Transplant or heart failure hospitalization
- Time to all-cause death or first heart failure hospitalization
- Cumulative heart failure hospitalizations
- Time to first heart failure hospitalization
- Modified Primary Effectiveness Endpoint including all-cause death, LVAD/Transplant, HF Hospitalizations, and worsening HF events treated as an outpatient but without KCCQ
- 6MWT changes from Baseline to 12 months

Additional Effectiveness Outcome Measurements:

- NYHA Class
- Patient Global Assessment
- Combined all-cause death and all-cause hospitalizations
- All-cause death
- Time to all-cause death (KM analysis)
- Time to cardiovascular death (KM analysis)
- Time to all-cause death, transplant or LVAD (KM analysis)
- Time to cardiovascular death, transplant or LVAD (KM analysis)

- Days alive free from heart failure hospitalization

- Outpatient Clinic HF Visit and / or intensification of heart failure therapy

- Emergency room HF visits

- HF Clinical Composite Assessment (improved, unchanged, or worsened) as described by Packer comprised of all-cause mortality, HF hospitalization, and changes in NYHA functional class ranking and Patient Global Assessment

- Comparison of transthoracic echocardiographic parameters as listed in Echocardiography Core Laboratory Manual

- Incidence of loss of shunt flow as measured on TTE and/or TEE

- Changes in 6MWT

- Death: All-cause; Cardiovascular cause (with breakdown by cause,e.g. sudden death, myocardial infarction, pump failure, stroke);Non-Cardiovascular cause; Undetermined cause; and relationship to device, study intervention or other cardiovascular procedure

- Hospitalization: All-cause; HF hospitalization, Non-HF hospitalization (with breakdown for cause including if associated
with secondary worsening of HF)

- Change in renal function

- Medication utilization including type, dose, frequency and changes

- Cost and cost-effectiveness data

- Technical success defined as successful delivery and deployment of the shunt and removal of the delivery catheter

- Technical success

- Device success

- Procedural success

- For Roll-in patients, transesophageal echocardiography at 6 and 12 months to assess shunt patency and other parameters as listed in the Echocardiography Core Laboratory Manual

Additional Safety Data Collection:

- Major Adverse Cardiovascular and Neurological Events (MACNE) and Bleeding Academic Research Consortium (BARC) types 3 and 5 bleeding at 30 days
- Percentage of Treatment Group patients with device-related MACNE at 12 months
- Incidence of all Serious Adverse Events by type at study duration
- Incidence of cerebrovascular events at study duration with sub-classification of CNS infarction, CNS hemorrhage, and TIA and their relationship to device or study procedures (per NeuroARC)
- Incidence of MI events at study duration after implantation
- Incidence of systemic embolization events at study duration after implantation
- Incidence of pulmonary embolism events at study duration after implantation
- Incidence of shunt implant embolization at study duration
- Device-related MACNE annually through 5 years
- Study device related MACNE in Shunt treated patients receiving LVADs for 5-year post study device implantation.

Study description

Background summary

HF is defined as the pathophysiologic state where the heart requires an elevated diastolic filling pressure to be able to pump blood adequately to meet the requirements of the metabolizing tissues or where the ability to eject blood is reduced. The underlying etiologies of HF are most commonly ischemic heart disease, hypertension, diabetes mellitus, idiopathic cardiomyopathy, valvular heart disease, myocarditis, followed by a host of other less common causes. While traditionally associated with reduced left ventricular (LV) systolic function, it is now widely recognized that HF can occur with normal or mildly reduced LV ejection fraction. Left heart failure is often divided into two clinical syndromes: systolic heart
failure or heart failure with reduced ejection fraction (HFrEF), and diastolic heart failure or heart failure with preserved ejection fraction (HFpEF), where the left ventricle fails to relax and fill normally (diastolic dysfunction). Patients with HFpEF tend to be older, are more commonly female, hypertensive and diabetic. The prevalence of patients with HFpEF presenting to hospital with ADHF is growing and is now approximately equally split with or in some cases surpassing HFrEF.

Study objective

The objective of the RELIEVE-HF study is to provide reasonable assurance of safety and effectiveness of the V-Wave Interatrial Shunt System by improving meaningful clinical outcomes in patients with NYHA functional class II, class III or ambulatory class IV heart failure, irrespective of left ventricular ejection fraction, who at baseline are treated with guideline-directed drug and device therapies.

Study design

The study is a prospective, multi-center, 1:1 randomized, patient and observer blinded trial, with a Shunt Treatment arm and a non-implant
Control arm. A total of approximately 400 patients will be randomized, with a possible increase up to a total of approximately 600 randomized patients based (total of 700 patients in the entire study, including 100 roll-in patients) on the results of a planned interim analysis. Each site may implant up to 2 Roll-in patients before randomizing to become familiar with the device and procedures (The Roll-in arm will be closed once 100 patients have been enrolled). The primary analysis will be performed when the last enrolled patient has been followed for a minimum of 12 months from randomization. The duration of follow-up evaluated by the primary effectiveness endpoint will range from a minimum of 12 to a maximum of 24 months. All implanted patients

(Roll-Ins, Randomized to Treatment and Control patients that cross-over and receive the shunt) will be followed for a total of 5 years from the time of the Study Device implantation.

Patients are enrolled after successful two-phase screening. Up to 2 patients per site are enrolled into the open-label Roll-in arm where they are implanted with shunts, cases are proctored, and patients are followed as per the Randomized cohort with the addition of TEEs done at 6 and 12 months to evaluate shunt patency. One to one patient randomization begins into the Shunt and Control arms. All patients receive GDMT. Control patients may cross-over to the treatment arm and receive the shunt device at the end of their 24-month follow-up or when the last patient reaches 12 months, if they consent and meet all study eligibility criteria again. Cross-over patients who receive the Shunt will be followed for 12 months according to the follow-up schedule described for the first 12 months post randomization. All patients implanted with shunts are followed annually for a total of 5 years from time of enrollment.

Intervention

The Study Device, the V-Wave Interatrial Shunt System, includes a permanent implant*the Shunt, placed during a minimally invasive cardiac catheterization procedure using its dedicated Delivery Catheter. By transferring blood from the left to the right atrium, the Shunt is intended to reduce excessive left-sided cardiac filling pressures in patients with advanced heart failure (HF). The anticipated outcomes are a reduction in symptoms related to pulmonary congestion including breathlessness, improved exercise capacity, and reduced need for hospitalization or emergency treatment for acute decompensated heart failure (ADHF).

Study burden and risks

Implanting permanent devices in the heart, especially within the left atrium and creating intracardiac shunts, carries with it known risks or complications, some of which may be severe, even at times fatal. Medical and/or surgical interventions may be required to correct clinical complications associated with the V-Wave Interatrial Shunt System and its implantation procedure. These known risks were considered
with respect to severity and frequency and addressed by V-Wave according to its risk management procedures as specified under the EN ISO 14971:2012 standard. Specifically, a Failure Mode and Effects Analysis process was conducted beginning with design initiation and revised throughout the development process. Wherever possible, design changes, methods of use, and training, have been adopted to mitigate the frequency and severity of these identified risks. As with any investigational device, there may be unforeseeable risks, which are not yet known at this time.

The potential risks are divided into 3 categories (See 'E9 What risks does participation involve for human subjects?')

The following list summarizes major anticipated adverse events that may result from the V-Wave Shunt, its implantation, or ancillary investigational protocol specified procedures. This list is not intended to be exhaustive. There may be other device or study procedure risks that are reasonably supported by the literature or expert consensus as foreseeable or anticipated risks.

- Abnormal laboratory results
- Acute decompensated heart failure
- Allergy, anaphylactic reaction, drug reaction, to contrast medium, anesthesia reaction, device components
- Arrhythmia
- Atrial septal defect (iatrogenic)
- Bleeding
- Cardiac arrest
- Cardiac or great vessel perforation
- Cardiac tamponade
- Coagulopathy
- Damage to adjacent cardiac structures
- Death
- Deep venous thrombosis (DVT)
- Device migration, embolization or erosion
- Device thrombosis
- Dislodgement of other previously implanted devices
- Effusion (e.g., pericardial, pleural, ascites)
- Emboli (air, thrombus, device)
- Emergency cardiac or vascular surgery
- Esophageal irritation, bleeding, perforation, or stricture
- Failure to deliver interatrial shunt to its intended site
- Failure to retrieve delivery system components
- Fever or hyperthermia
- Gastrointestinal disturbance (tear of bleeding of esophagus, peritonitis, infarction, ileus, nausea, vomiting, diarrhea)
- Hematuria
- Hemolysis
- Hemoptysis
- Hemorrhage requiring transfusion
- Hypertension
- Hypotension
- Hypoxemia
- Infection (including septicemia and endocarditis)
- Interference with other implanted devices
- Loss of limb
- Myocardial infarction
- Nerve damage

- Pain
- Permanent disability
- Pneumothorax
- Pulmonary thromboembolism
- Radiation induced skin or tissue injury
- Reintervention/closure of shunt due to excessive shunting
- Removal of shunt due to infection
- Renal insufficiency
- Respiratory failure, atelectasis, pneumonia
- Seizure
- Shock (cardiogenic or anaphylactic)
- Skin irritation or inflammation
- Stridor
- Stroke or transient ischemic attack (TIA)
- Syncope
- Thrombosis
- Urinary retention
- Urinary tract infection
- Vascular trauma (dissection, occlusion, hematoma, arteriovenous fistula, pseudoaneurysm, perforation, spasm)
- Worsening right ventricular heart failure and pulmonary hypertension

The potential benefits to patients implanted with the V-Wave Shunt include:
- Serial evaluation, close monitoring, and medical optimization by cardiologist and skilled heart failure team
- Reduction in the severity and frequency of heart failure symptoms such as dyspnea
- Improvement in quality of life
- Improvement in exercise capacity
- Reduction in the number of hospitalizations for worsening heart failure
- Reduction in the number of Emergency Room visits for worsening heart failure
- Reduction in the number of urgent clinic visits of worsening heart failure
- Prolongation of life

The potential benefits to patients not implanted with the Shunt (Controls) include:
- Serial evaluation, close monitoring, and medical optimization by cardiologist and skilled heart failure team
- Opportunity to receive the Shunt after unblinding (maximum of 24 months)

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Ischemic or non-ischemic cardiomyopathy with either reduced or preserved LV ejection fraction and documented heart failure for at least 6 months from baseline visit.
2.NYHA Class II, Class III or ambulatory Class IV HF (historical assessment documented at the Baseline Screening visit).
3. Receiving guideline directed medical therapy (GDMT) for heart failure which refers to those HF drugs carrying a Class I indication:
a) Patients with reduced LVEF (<=40%): An inhibitor of the renin-angiotensin system (RAS inhibitor), including an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) or angiotensin receptor-neprilysin inhibitor (ARNI) and a beta-blocker (BB), for at least 3 months prior to the Baseline Visit.
b) Patients with reduced LVEF (<=40%): Other medications recommended for selected populations, e.g., mineralocorticoid receptor antagonist (MRA) or nitrates/hydralazine should be used in appropriate patients, according to the published guidelines.
c) All patients: Patient has been on stable HF medications, as determined by the investigator, for at least 1 month , with the exception of diuretic

therapy. Stable is defined as no more than a 100% increase or 50% decrease in dose within these periods.
d) All patients: Drug intolerance, contraindications, or lack of indications must be attested to by the investigator. Patients should be on appropriate doses of diuretics as required for volume control.
4. Receiving Class I recommended cardiac rhythm management device therapy. Specifically: if indicated by class I guidelines, cardiac resynchronization therapy (CRT), implanted cardioverter-defibrillator (ICD) or a pacemaker should be implanted at least 3 months prior to
Baseline Visit. These criteria may be waived if a patient is clinically contraindicated for these therapies or refuses them and must be attested to by the investigator.
5. NYHA Class II must meet both 5a AND 5b. NYHA Class III and ambulatory Class IV must meet 5a OR 5b.
a) One (1) prior Heart Failure Hospitalization with duration >24 hours or Emergency Room Heart Failure Visit with duration >=6 hours, or Heart Failure Clinic ADHF Visit with duration >=6 hours, within 12 months from Baseline Visit.
i) If a CRT device was previously implanted, the heart failure hospitalization must be >= 1 month after CRT implantation.
ii) If a mitral valve repair device (e.g. MitraClip) was previously implanted, the heart failure hospitalization must be >= 1 month after mitral valve repair implantation.
b) Alternatively, if patients have not had a HF hospitalization or ER HF Visit within the prior 12 months, they must have a corrected elevated Brain Natriuretic Peptide (BNP) level of at least 300 pg/ml or an N-terminal pro-BNP (NT-proBNP) level of at least 1,500 pg/ml, according to local measurement, within 3 months of the Baseline Visit during a clinically stable period and at least 1 month after implantation of a CRT or mitral valve repair devices. (Note: "corrected" refers to a 4% reduction in the BNP or NT-proBNP cutoff for every increase of 1 kg/m2 in BMI above a reference BMI of 20 kg/m2). If patient is on ARNI, NT-proBNP should be used exclusively.
6. Able to perform the 6-minute walk test with a distance >=100 meters and <=450 meters. The test will be performed twice separated by a minimum of 60 minutes between tests. The second test may be performed up to 7 days after the first test, if needed. The higher reading shall be used as the baseline value.
7. Provide written informed consent for study participation and be willing and able to comply with the required tests, treatment instructions and follow-up visits.

Exclusion criteria

1. Age <18 years old.
2. BMI >45 or <18 kg/m2.
3. Females of childbearing age who are not on contraceptives or surgically sterile, pregnant or lactating mothers.

4. Resting systolic blood pressure <90 or >160 mmHg after repeated measurements.
5. Baseline echocardiographic evidence of unresolved, non-organized or mobile intracardiac thrombus.
6. Severe pulmonary hypertension defined as PA systolic pressure >70 mmHg by echo/Doppler (or PVR >4.0 Wood Units by PA catheter measurement that cannot be reduced to <=4 Wood Units by vasodilator therapy).
7. RV dysfunction defined as TAPSE <12mm or RVFAC <=25% as assessed on Baseline TTE.
8. Left Ventricular End-Diastolic Diameter (LVEDD) >8cm as assessed on Baseline TTE.
9. Atrial septal defect (congenital or iatrogenic), patent foramen ovale, or anomalous pulmonary venous return, with more than trace shunting on color Doppler or intravenous saline contrast (bubble study) or prior surgical or interventional correction of congenital heart disease
involving the atrial septum (excluding closure by suture only but including placement of a PFO or ASD closure device).
10. Untreated moderately severe or severe aortic or mitral stenosis.
11. Untreated severe or greater regurgitant valve lesions, which are anticipated to require surgical or percutaneous intervention within 12 months.
12. Mitral valve repair device (e.g. MitraClip) implanted within 3 months prior to Baseline Visit.
13. Untreated coronary stenosis which requires surgical or percutaneous intervention.
14. Acute MI, acute coronary syndrome (ACS), percutaneous coronary intervention (PCI), rhythm management system revision,(not including generator change) lead extraction, or cardiac or other major surgery within 3 months of baseline visit. Rhythm management system generator change within 1 month of Baseline Visit.
15. Known active valvular vegetations, atrial myxoma, hypertrophic cardiomyopathy with significant resting or provoked subaortic gradient, acute myocarditis, tamponade, or large pericardial effusion,
constrictive pericarditis, infiltrative cardiomyopathy (including cardiac sarcoidosis, amyloidosis, and hemochromatosis), or congenital heart disease, as cause of HF.
16. Stroke, transient ischemic attack (TIA), systemic or pulmonary thromboembolism, or deep vein thrombosis (DVT) within 6 months of Baseline Visit. Any prior stroke with permanent neurologic deficit. Existing IVC filter.
17. Transseptal procedure for another indication (e.g. AF ablation, left atrial appendage occlusion, mitral valve repair/replacement) anticipated within 6 months.
18. Bradycardia with heart rate <45 bpm (unless treated with a permanent pacemaker) or uncontrolled tachyarrhythmias. This includes defibrillation shocks reported by the patient within 30 days from baseline visit.
19. Intractable HF with:
a) Resting symptoms despite maximal medical therapy (ACC/AHA HF Stage D).

b) Treatment with IV vasoactive medications (e.g., IV inotropes, IV vasodilators) within the last 30 days.
c) Cardiac Index <1.5 L/min/m2.
d) Treated with a ventricular assist device (VAD).
e) Listed for cardiac transplantation.
20. Prior cardiac transplantation.
21. Patients with HFrEF (LVEF <=40%) who are intolerant to a RAS inhibitor including all of ACEI, ARB or ARNI, and intolerant to beta-blocker medical therapy.
22. Not eligible for emergency cardiothoracic or vascular surgery in the event of cardiac perforation or other serious complication during study intervention procedure.
23. Life expectancy <1 year due to non-cardiovascular illness.
24. Coagulopathy or is taking anticoagulation therapy which cannot be interrupted for the study intervention procedure, or has contraindications for all of the study-mandated post
implantation anticoagulation / antiplatelet regimens or known hypersensitivity, or contraindication to procedural medications which cannot be adequately managed medically.
25. Estimated glomerular filtration rate (eGFR) <25 ml/min/1.73 m2 by the MDRD method, or not responsive to diuretics, or is receiving dialysis.
26. Hepatic impairment with a documented liver function test result (transaminases, total bilirubin, or alkaline phosphatase) >= 3 times upper limit of normal.
27. Severe chronic pulmonary disease requiring daytime home oxygen or chronic oral steroid therapy (Note: nighttime oxygen therapy and inhaled steroid therapy are acceptable).
28. Active infection requiring parenteral or oral antibiotics.
29. Known allergy to nickel.
30. Any condition that may interfere with compliance of all protocol procedures, such as active drug addiction, active alcohol abuse, or psychiatric hospital admission for psychosis within the prior year.
31. Currently participating in a clinical trial of any investigational drug or device that has not reached its primary endpoint, or any study that may interfere with the procedures or endpoints of this trial.
Participation in an observational study or registry with market approved drugs or devices would not exclude a patient from participation in this trial.
32. Patient is otherwise not appropriate for the study as determined by the investigator or the Eligibility Committee, for which the reasons must be documented.
33. Patient belongs to a vulnerable population per investigator*s judgment or patient has any kind of disorder that compromises his/her ability to give written informed consent and/or to comply with study procedures.
Final Exclusion Criteria (FEC): Assessed during cardiac catheterization, at Study Intervention Visit, just prior to Randomization:
1. Change in clinical status between baseline screening and Study Intervention visit such that the patient is not stable to undergo the Intervention

Procedure.
2. Females with a positive pregnancy test on laboratory testing for FEC.
3. Unable to undergo TEE or ICE.
4. Unable to tolerate or cooperate with general anesthesia or conscious sedation.
5. Anatomical anomaly on TEE or ICE that precludes implantation of Shunt across fossa ovalis (FO) of the interatrial septum including:
a) Minimal FO Thickness >6mm in and adjacent to the location intended for shunt placement
b) Minimal FO Length <10mm.
c) ASD or PFO with more than a trace amount of shunting.
d) Intracardiac thrombus felt to be acute and not present on prior exams.
e) Atrial Septal Aneurysm defined as >= 10 mm of phasic septal excursion into either atrium or a sum total excursion of >= 15 mm during the cardiorespiratory cycle, with a base of >= 15 mm.
6. Inadequate vascular access for implantation of Shunt. Femoral venous or inferior vena cava (IVC) access for transseptal catheterization are not patent as demonstrated by failure to pass Swan-Ganz or ICE catheter from the right or left femoral vein to the right atrium.
7. Hemodynamic, heart rhythm, or respiratory instability at time of cardiac catheterization including:
a) Mean PCWP <7 mmHg, not correctable by IV volume infusion (maximum 1,000 ml normal saline or equivalent).
b) Mean PCWP >35 mmHg, not correctable by medical therapy (e.g. IV Furosemide, IV or sublingual nitroglycerin).
c) Right Atrial Pressure (RAP) >= Left Atrial Pressure (LAP or PCWP) when LAP (PCWP) >=7 mmHg.
d) Cardiac Index (CI) <1.5 liters/min/m2 after correction of volume depletion with IV fluids (maximum 1,000 ml normal saline or equivalent).
e) Severe pulmonary hypertension defined as PASP >70 mmHg associated with PVR >4.0 Wood Units that cannot be reduced to PVR <=4 Wood Units by acute vasodilator therapy.
f) Resting systolic Blood Pressure <90 or >160 mmHg, not corrected with IV fluid administration or vasodilators, respectively.
g)Need for IV infusions of vasopressor or inotropic medication. Transient hypotension or bradycardia during anesthesia or catheterization, manifest as a vagal or similar acute episode or dehydration, responding promptly to IV fluid boluses or

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-07-2020
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	V-Wave Interatrial Shunt System
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	15-11-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	02-01-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	28-01-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	18-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-07-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-10-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-03-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-08-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-10-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
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Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-04-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	24-08-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-02-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-10-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
ClinicalTrials.gov	NCT03499236
CCMO	NL65638.100.18