A prospective, double blind, randomized, placebo-controlled clinical trial of intracoronary infusion of immunoselected, bone marrow-derived Stro3 mesenchymal precursor cells (MPC) in the treatment of patients with ST-elevation myocardial infarction

Published: 26-09-2011
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Primary Objective:• To determine the safety and feasibility of intracoronary allogeneic, immuno-selected, bone marrow-derived Stro3 MPC delivery in the treatment of subjects with STEMI undergoing PCI of the LAD coronary artery.Secondary Objectives...

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

Summary

ID

NL-OMON45102

Source
ToetsingOnline

Brief title
The AMICI trial

Condition

- Myocardial disorders

Synonym
heart attack, ST-elevation myocardial infarction

Research involving
Human

Sponsors and support

Primary sponsor: Mesoblast Inc
Source(s) of monetary or material Support: Mesoblast;Inc. (voorheen Angioblast Systems Inc.)

Intervention

Keyword: Acute myocardial infarction, allogeneic, intracoronary, Mesenchymal stem cells

Outcome measures

Primary outcome

Feasibility endpoint: Feasibility of the infusion of the investigational agent

will be monitored by measurement of TIMI flow and perfusion prior to, during

(approximately 50% of total investigational agent volume infused), and

following the investigational agent infusion after successful PCI and stenting.

Primary Efficacy Endpoint:

The primary efficacy endpoint is the change in LV end-systolic volume (LVESV)

as assessed by cardiac MRI from baseline to 6 months post investigational agent

infusion in each MPC treatment group compared with the Placebo group.

Safety endpoint: All safety end points will be assessed from patient

randomization through 24 months post investigational agent infusion:

- Serious adverse events (SAEs) / adverse events (AEs) rates

- Occurrence of MACCE including cardiovascular death, non-fatal myocardial

infarction, non-fatal stroke, and cardiac hospitalization due to heart failure.

cardiac death, myocardial infarction, target vessel revascularization, stroke, new or worsening congestive heart failure during index hospitalization and cardiac hospitalizations due to congestive heart failure

- Target vessel (or other vessel) revascularization post index cardiac catheterization and new or worsening heart failure during the index hospitalization will be tracked as "Adverse Events of Special Interest".

- Total number of subjects with documented ventricular arrhythmia (sustained and non-sustained VT/VF) throughout the study period

- Angina pectoris as defined by Canadian Cardiovascular Society (CCS) clinical clarification

- New York Heart Association (NYHA) Class

-Telemetry/48 hour Holter monitoring (during hospital admission and at 14 and 30 days, 3 and 6 months follow-up time points) with assessment of occurrence of ventricular arrythmia

- TIMI flow and perfusion measurements following intracoronary infusion of the MPC cell solution compared with placebo

- Physical examinations, monitoring of vital signs (heart rate, respiratory rate, BP, and oral temperature)

- Results of clinical laboratory tests (hematology, serum chemistry, inflammatory markers), and immunogenicity assays; (flow cytometry Class I and Class II HLA percent reactivity % with specificity, antibovine and antimurine antibody analysis)

Secondary outcome

Secondary Efficacy Endpoints:

- The change in LVESV as assessed by 2D-echocardiography from baseline to 6 months post investigational agent infusion.

- The change in relative infarct size as assessed by late contrast enhancement MRI (% infarct volume/total LV tissue volume) from baseline to 6 months post investigational agent infusion.

- Additional functional efficacy endpoints will be assessed with the following diagnostic studies:

o Cardiac MRI at days 2-4 and 30; month 6

o LVEF

o LV-ESV

o LV-EDV

o Left ventricular wall thickness and thickening in all segments including infarct area

o Regional wall motion score

o Myocardial microvascular obstruction measured as reduced signal intensity in the region of interest

o MI size measured in the region of interest as late contrast enhancement

o Myocardial salvage index

o 2D echocardiogram at days 2-4 and 30; month 6

o LVEF

o LVESV

o LVEDV

o Cardiac dimensions (LVESD/ LVEDD)

o Regional wall motion score index

- If there is no difference between the MPC groups (using a test with alpha = 0.1) in the effect on LVESV then the pooled MPC group will be compared to the Placebo group for all functional parameters.

- A subset analysis that corresponds to the stratification used during randomization will be performed.

Stratification will be based on the following categories defined as time from onset of AMI symptoms to PCI:

o <=2 hours

o >2 to <=6 hours

o >6 to <=12 hours.

- In addition, a subset analysis will be evaluated at the following ischemia duration time points:

o <=6 hours

o >6 to <=12 hours

- NT-Pro-BNP serum levels (as a biomarker for heart failure) at baseline, days 2-4 and 30, and months 3, 6, 12 and 24

- Score changes for TIMI Flow Grade and TIMI Myocardial Perfusion Grade assessments at the following day 0 time points:

o pre-PCI,

o immediately post-PCI,

o after approximately 50% of intracoronary infusion of investigational

agent,

o at completion of intracoronary infusion of investigational agent.

Study description

Background summary

Healing of an MI is complicated by the need for viable myocytes at the peri-infarct margin to undergo compensatory hypertrophy in order to increase pump function in response to the loss of infarcted tissue. This initiates a process termed *cardiac remodeling,* which is characterized by apoptotic loss of hypertrophied myocytes, expansion of the initial infarct area, progressive collagen replacement, that collectively result in the development of heart failure. The Sponsor has recently advanced the hypothesis that hypertrophied cardiac myocytes undergo apoptosis because the endogenous capillary network cannot provide the compensatory increase in perfusion required for cell survival. Vascular network formation is the end result of a complex process that begins in the prenatal period with induction of vasculogenesis. Cells that can differentiate into endothelial and smooth muscle elements also exist in adult bone marrow12-14 and can induce vasculogenesis in ischemic tissues. The Sponsor has identified a specific population of MPCs derived from human adult bone marrow which has phenotypic and functional characteristics of vascular pericyte precursor cells that provide the building blocks necessary for arteriogenesis. Since recent observations
have suggested that a second compensatory response of viable cardiomyocytes is to proliferate and regenerate following injury. It is theoretically possible that further increase in the infarct bed capillary network through regulated neovascularization could result in increased regenerative capacity of the heart leading to improvement in myocardial function. Administration of MPCs resulted in significant improvement in several key parameters of myocardial function in rodents following AMI. In particular, epicardial injection of MPCs resulted in a dose-dependent arteriogenesis at the infarct border zone. This arteriogenesis was coupled with echocardiographic improvement in EF as well as restoration of near normal contractility and LV end-diastolic pressure. Additionally, MPCs have been shown to secrete cytokines in a paracrine manner that could augment their direct trans differentiation potential. The use of the *off-the-shelf* allogeneic MPCs derived from healthy donors with the Sponsor*s proprietary process requires no cell culture and can be infused directly following recanulation of the involved artery and reperfusion of the infarcted tissue during a time period of myocardial infarction. The use of allogeneic donor cells obviates the need for second catheterization, hospitalization or

anesthetic for treatment. Therapy can be provided without the delay, necessitated by days or weeks of cell culture, commonly observed with the use of mesenchymal stem cells obtained from bone marrow.
Furthermore, the Sponsor has demonstrated, in clinical trials using allogeneic MPCs, that the therapy is safe and potentially effective in restoring cardiac function. This study will, for the first time, investigate the use of intra-coronary delivery of an allogeneic mesenchymal stem cell product in a subject demographic undergoing standard of care percutaneous coronary intervention following AMI.
By combining an allogeneic, off-the-shelf, cell-based therapy, with intracoronary delivery, the Sponsor seeks to investigate a treatment that aims to limit the progression of heart failure and increase overall survival and quality of life.

Study objective

Primary Objective:
• To determine the safety and feasibility of intracoronary allogeneic, immuno-selected, bone marrow-derived Stro3 MPC delivery in the treatment of subjects with STEMI undergoing PCI of the LAD coronary artery.
Secondary Objectives:
• To explore a dose-response effect of intracoronary delivered MPC in the treatment of subjects with an anterior wall STEMI on LV remodelling, microvascular obstruction, and the relationship between time from onset of ischemic symptoms to primary PCI.
• To determine the effect of intracoronary delivery of allogeneic immunoselected, bone marrow-derived MPC, on infarct size reduction in the treatment of subjects with STEMI undergoing primary PCI of the LAD coronary artery.
• To explore additional functional and clinical effects of MPC in STEMI.

Study design

This is a Phase 2, prospective, double-blind, randomized, placebo-controlled, dose finding study that will enroll approximately 105 subjects with de novo anterior STEMI due to a lesion involving the left anterior descending (LAD) coronary artery who undergo primary PCI at approximately 25 clinical study sites.
The study will enroll three parallel treatment arms of 35 subjects each, as follows:
- Intracoronary infusion of 12.5 x10^6 MPCs suspended in 100 mL 0.9% saline
- Intracoronary infusion of 25 x 10^6 MPCs suspended in 100 mL 0.9% saline
- Intracoronary infusion of 100 mL 0.9% saline (placebo control treatment).
Potential subjects will be approached by the site investigator and provided first with an informed consent form for signature. Following successful and uneventful PCI, the subjects will be randomized.

Once the subject has been randomized, the stented left anterior descending artery supplying the area of the heart with the infarction will be infused with either the saline placebo solution or the allogeneic MPC(RevascorTM) product via an approved percutaneous infusion microcatheter (e.g. Twin Pass).
The subjects randomized to MPCs will be infused at an infusion rate of 2 ml/min over a 50 min period (2.5x10^5 MPCs/min (12.5 M), 5.0x10^5 MPCs/min (25 M)).
The subjects randomized to placebo will be infused placebo solution at 2 mL/min over a 50 min period (0 MPCs/min). The MPC product (12.5M and 25M MPCs) and the placebo solution will be diluted in 100mL 0.9% saline prior to infusion.
The Sponsor will provide all sites with blinded treatment bags, which contain the different doses of MPCs or placebo solution.
An intracoronary (IC) bolus of glyceryl trinitrate (GTN)/ nitroglycerin (NTG) (100-200 mcg) should be administered (blood pressure permitting) prior to the initial infusion of the investigational agent. Additionally, a similar dose of intracoronary GTN (NTG) should be given prior to TIMI flow assessment during the investigational agent infusion period as well as after completion of the investigational agent infusion and immediately prior to the final coronary angiographic imaging.
After approximately 50% of the intracoronary infusion of investigational agent has been completed, an angiographic determination of coronary flow will be performed. The remaining investigational agent should be infused if either TIMI 2 or TIMI 3 flow is present and ALL of the following are absent:
o Sustained hypotension not responsive to fluid administration;
o Clinical signs/symptoms indicating an acute cerebrovascular event;
o Re-elevation of ST-segments if previously resolved with PCI;
o Onset of the subject*s symptoms of myocardial ischemia unresponsive to appropriate interventions;
o Two episodes of sustained ventricular tachycardia (VT)/ventricular fibrillation (VF) requiring cardioversion (infusion can continue if a single episode of sustained VT/VF requiring cardioversion occurred).
If for any reason, the site investigator withdraws a randomized subject prior to infusion of the investigational agent, the reason for early termination and date from the screening visit will be entered into the eCRF by the study site. The subject will not remain in the study. If for any reason, a subject*s study infusion is halted due to safety considerations, the subject will remain in the study. A subject who prematurely withdraws from the study, post-study infusion will remain in the study. All subjects will undergo cardiac imaging and functional studies, clinical evaluations, and laboratory testing.
An independent Data Safety and Monitoring Board (DSMB) will review all relevant acute periprocedural data, serious adverse events, other adverse events, and efficacy data (if requested) periodically dependent on subject enrollment, and advise the Executive Steering Committee (ESC) regarding the progression of the study. An ESC will oversee all aspects of the study. The ESC will consist of the Principal Investigator, site investigators and representatives from the Sponsor.
A Clinical Events Committee (CEC) will review appropriate source documents and adjudicate (blinded per a priori procedure) all MACCE (Major adverse cardiac

and cerebrovascular events) defined as cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or cardiac hospitalization due to heart failure. Target vessel (or other vessel) revascularization post index cardiac catheterization and new or worsening heart failure during the index hospitalization will be tracked as "Adverse Events of Special Interest" rather than MACCE.
The investigators, subjects, and sponsor will remain blinded for study allocation of the individual subjects for the duration of the study (24 months). The DSMB may choose to be unblinded. The DSMB safety reviews to assess the frequency of total major adverse cardiac and cerebrovascular events (MACCE), which will be performed after the initial 15, 30, 60, and 90 subjects have been observed at Day 30 post the index cardiac catheterization.

Intervention

Intracoronary infusion of Stro-3 mesenchymal precursor cells after revascularisation of the culprit coronary artery

Study burden and risks

There are certain known and expected risks associated with products that are used in the production of RevascorTM as well as expected risks with cardiac catheterization, cMRI, echocardiography, and blood draws. These risks are detailed in the sections that follow.

Reaction to Fetal Calf Serum or Murine Mouse Antibody: For immunoselection of the allogeneic MPCs, the technology incorporates an antibody based sorting process using murine derived antihuman antibody. In the cell expansion process, fetal calf serum is used. It is based on these 2 processes that subjects with known hypersensitivity to murine and/or bovine products are excluded from study participation. Acceptable study
candidates will be required to undergo serum collection and monitoring for the potential development of antimurine antibodies and antibovine antibodies, respectively, and they will be monitored for the clinical significance of these antibodies, if any. The risk of sensitization from
this formulation is unknown, but expected to be extremely rare. If sensitization occurs, subsequent therapies containing bovine or murine products may not be made available to study subjects.

Reaction to Dimethyl Sulfoxide
Dimethyl sulfoxide 7.5% is used as part of the RevascorTM cryopreservation process. The therapeutic and toxic effects of DMSO include its own rapid penetration and enhanced penetration of other substances across biologic membranes, free radical scavenging, and effects on coagulation, anticholinesterase activity, and DMSO-induced histamine release by mast cells. The systemic toxicity of DMSO is considered to be low. The DMSO exposure in

this therapy is minimal and is locally applied. Subjects with known hypersensitivity to DMSO will be excluded from the study.

Potential Cell Contamination

RevascorTM is an allogeneic, immunoselected, ex vivo expanded cell product, which has the potential to become contaminated and subsequently cause infection in the study subject at the time of surgical implantation. This risk is greatly minimized by the use of a Good Manufacturing Practice (GMP)-compliant production facility. Prior to the release of RevascorTM from the GMP facility, rigorous screening tests for multiple infections agents are performed in order to ensure that no contaminated product is released for use. As with any blood or marrow derived biological agent, infectious risks from unknown pathogens are possible.

Potential Inflammatory Responses

The administration of allogeneic MPCs may elicit immunogenic and/or inflammatory responses resulting from allogeneic exposure to the donor cells and/or manufacturing content. To date, no clinical signs or symptoms have been associated with the development of antibodies to HLA, bovine, or murine proteins. The risks of exposure are not fully known but there is a remote potential risk that subsequent allogeneic transplant donor selection may be limited in the presence of persistent, cross-match reactive anti-HLA antibodies. Subjects will be monitored for these responses by performing antibody screening tests to HLA, bovine, and murine antibodies at designated follow-up visits.

Possible Effects of Cells on the Fetus

Because of potential or unknown side effects of the study on the fetus, if the subject is a female of childbearing potential, the subject must have a negative urine pregnancy test prior to study entry. In addition, females of childbearing potential will be included in study participation provided that she is willing to use adequate contraception (hormonal pill, implant or intrauterine device, barrier methods only if used consistently) from the time of screening and for a period of at least 16 weeks after surgery.

Cardiac Catheterization and PCI

The risk of producing a major complication during cardiac catheterization is reported well below 1%. Some of the potential complications during cardiac catheterization may include death; MI; stroke and transient ischemic attack; vascular complications including bleeding, hematoma, acute thrombosis, distal embolization, pseudo aneurysm, arteriovenous fistula; arrhythmias; perforation of the heart or great vessels; allergic reactions; atheroembolism; acute renal failure; infection; radiation exposure. Potential complications related more specifically to stenting can include failure of stent deployment and stent thrombosis. The contrast agent injected during these procedures may create a sensation of warmth and/or pain. Other adverse events experienced by <1% of

subjects include things such as hives, sneezing, coughing, hypotension, hypertension, arrhythmias, anginal symptoms, shivers, collapse, anxiousness, confusion, blurred vision, taste sensation, headache, fever and chills.

cMRI
The MRI scan itself is painless, but it may cause some people to feel claustrophobic. There is a small risk of an allergic reaction to the contrast agent. MR imaging may be performed with either dipyridamole or adenosine and both cause coronary vasodilation therefore they can cause some transient side effects. The most common side effects of dipyridamole administration are chest discomfort and headache. The most common side effects of adenosine administration are chest discomfort, headache, dyspnea, and flushing. In addition nausea, low blood pressure, and rarely, heart block have been experienced during adenosine administration.

Echocardiogram
Rarely, some subjects complain of discomfort to the skin where the ultrasound probe is pressed against the chest by the technician.

Electrocardiogram
The actual procedure for the ECG is safe with no known side effects. Occasionally there are complaints that the adhesive that the leads attach to cause slight skin irritation.

Laboratory or Blood Work
The risks for blood drawing are rare but possible as described by the following: pain at the needle insertion site, bleeding, bruising or a hematoma at the needle entry site, damage to surrounding tissue or nerves, fainting, nausea, and vomiting.
The total blood draw for this study is approximately 81 ml:
Baseline: 11 ml
Visit 3: 2 ml
Visit 4: 2 ml
Visit 5: 2 ml
Visit 6: 9 ml
Visit 7-12: 11 ml

Contacts

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US
Scientific
Mesoblast Inc

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US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Subjects will be entered into this study only if they meet ALL of the following criteria:
1.*Willing and able to understand and sign the Informed Consent Form (ICF).
2.*Males or females >= 18 years.
3.*Clinical symptoms consistent with AMI (pain, etc.) for a maximum
of 12 hours from onset of symptoms to completion of percutaneous coronary intervention (PCI).
4.*De novo anterior Acute Myocardial Infarct (AMI) defined as:
*>= 0.2 mV ST elevation in 2 or more V1 - V6 leads with presentation in a maximum of 12 hours of onset of symptoms.
Or:
Presumed new left bundle branch block with a minimum of 0.1 mV concordant ST elevation with presentation in a maximum of 12 hours of onset of symptoms.
And:
Occlusion or flow limiting lesion with TIMI Flow Grade 0 or 1 in the left anterior descending (LAD) coronary artery.
5.*Successful revascularization of the culprit lesion in the LAD within a maximum of 12 hours from
the onset of AMI symptoms defined as (1) primary percutaneous coronary intervention (PCI) with stent implantation, resulting in TIMI 3 or 2 flow AND (2) residual stenosis of less than 20%

by on-line QCA.
NOTE: Subject is eligible if in addition to requiring a primary PCI plus stenting for the culprit lesion they have a stenosis of the LAD that is both distinct from the culprit lesion and requires PCI at the time of the index cardiac catheterization procedure. For example, if the culprit lesion is in the mid LAD but there is also a high-grade first diagonal (D1) stenosis, then the latter lesion may undergo
PCI (plus stenting) during the index catheterization This specifically excludes patients who may require a PCI to a non-LAD coronary artery during the index catheterization.;6.*If a female subject is of childbearing potential (i.e not amenorrheic for 12 or more months and/or not surgically sterile), the subject must be willing to use a highly effective method of contraception (oral, injectable or implanted hormonal methods of contraception, placement of an intrauterine device [IUD] or intrauterine system [IUS], condom or occlusive cap with spermicidal foam/gel/film/cream/suppository, male sterilization, or true abstinence) for at least 16 weeks after investigational agent infusion.
7.*Must be willing and able to return for required follow-up visits.

Exclusion criteria

Subjects will not be enrolled into this study if they meet ANY of the following criteria:
1. Prior MI, known cardiomyopathy, or hospital admission for heart failure (HF)
2. Significant valvular disease (mitral or aortic valve regurgitation 3/4 classification as defined by ESC/ACC guidelines)
3. Unsuccessful revascularization of culprit artery defined as TIMI 1 or 0 flow or residual diameter stenosis of >= 20% by on line QCA analysis
4. Need for staged treatment of coronary artery disease, or other interventional or surgical procedures to treat heart disease (e.g., valve replacement, PCI or CABG) planned or scheduled within 6 months after infusion with the investigational agent. EXCEPT: Patients who present at the index catheterization with a need for a staged PCI of a non-LAD coronary artery will be eligible if:
* *The staged PCI vessel does not have important collaterals to the LAD, and
* *Agreement from the PI that the staged PCI can be safely scheduled after the day 30 cMRI has
been determined by the Core cMR Imaging Laboratory to satisfy quality-control criteria.
5. Cardiogenic shock or hemodynamic instability within 24 hours prior to randomization, defined as the presence of any of the following:
* Systolic blood pressure <80 mmHg lasting for more than 30 minutes
* Heart rate >120 bpm for more than 1 hour
6. Prior coronary artery bypass graft to the LAD
7. History of persistent atrial fibrillation
8. Prior PCI involving LAD
9. Malignancy within last 3 years from screening. The subject has had an active malignancy, within the past 3 years except for cervical carcinoma in situ and non-melanoma skin cancer that has been definitively treated
10. Acute or chronic bacterial or viral infectious disease
11. Pacemaker, ICD or any other contra-indication for cMRI. This is inclusive of patients with

an MRI compatible device that was implanted prior to the potential qualifying event.
12. Known history of severe chronic obstructive pulmonary Disease (Forced Expiratory Volume (FEV1) <35% in 1 second).
13. Known glomerular filtration rate (GFR) of less than 30 mL/min at study entry.
14. Known history of sensitization to human leukocyte antigens (such as via pregnancy, transfusions or organ transplant).
15. Known hypersensitivity to any radiographic contrast (e.g. gadolinium).
16. Known hypersensitivity to dimethyl zwaveloxide (DMSO), murine proteins, bovine proteins, acetylsalicylic acid (ASA), clopidogrel, prasugrel, and/or metallic stents
17. Prior or current participation in any bone marrow derived autologous and allogeneic stem cell or gene therapy study
18. Prior participation in any other investigational drug trial in the past 30 days.
19. Pregnant or lactating women
20. Intent to participate in any other investigational drug, cell or gene therapy study during the 2-
year follow-up period of this study
21. Any concurrent disease or condition that, in the opinion of the investigator, would make the subject unsuitable for participation in the study

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-05-2014
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cels allogenic

Ethics review

Approved WMO Date:	26-09-2011
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-04-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-06-2012
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-09-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-11-2012
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-01-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO	

Date:	29-03-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-05-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-10-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-10-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-11-2013
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-06-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Not approved Date:	17-07-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-08-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	06-11-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-11-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-12-2014
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-03-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-04-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-09-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-10-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-07-2017

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-10-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-12-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2010-020497-41-NL
CCMO	NL36947.000.11

Study results

Date completed:	01-01-1900
Results posted:	07-12-2023
Actual enrolment:	3

First publication
09-02-2023