A first-in-human, randomized, double-blind, placebo-controlled study to evaluate, single ascending doses of CIT-013 in healthy volunteers with and without an intravenous lipopolysaccharide challenge and repeat dosing in healthy volunteers and patients with Rheumatoid Arthritis.

Published: 27-05-2021
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Objectives Part A: • To evaluate the safety and tolerability of CIT-013 after administration of single, ascending, IV doses in healthy volunteers.• To evaluate the pharmacokinetics of CIT-013 after administration of single, ascending, IV doses in…

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON56333

Source
ToetsingOnline

Brief title
CIT013 First in Human study

Condition

- Other condition
- Autoimmune disorders

Synonym
Acute and chronic inflammatory disorders, Autoimmune disorders

Health condition

Acute and chronic inflammatory disorders and Rheumatic Arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Citryll
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Antibody, FIH, LPS, NETosis, RA, Rheumatoic Arthritis

Outcome measures

Primary outcome

Part A

• Treatment-emergent (serious) adverse events ((S)AEs) throughout the study at every study visit

• Concomitant medication throughout the study at every study visit

• Vital signs (Pulse Rate (bpm), Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg)) as per assessment schedule

• Clinical laboratory tests (Haematology, blood chemistry and urinalysis) as per assessment schedule

• ECG parameters (Heart Rate (HR) (bpm), PR, QRS, QT, QTcB, QTcF) as per assessment schedule

• PK parameters of CIT-013 by non-compartmental analysis of the serum

concentration-time data: Single ascending dose:

• AUCinf, AUClast, CL, Cmax, t1/2, tlag, tmax, Vz

• Dose-normalized PK parameters: AUCinf, AUClast, Cmax

Secondary outcome

Part B

• Treatment-emergent (serious) adverse events ((S)AEs) throughout the study at every study visit

• Concomitant medication throughout the study at every study visit

• Vital signs (Pulse Rate (bpm), Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg)) as per assessment schedule

• Clinical laboratory tests (Haematology, blood chemistry and urinalysis) as per assessment schedule

• ECG parameters (Heart Rate (HR) (bpm), PR, QRS, QT, QTcB, QTcF) as per assessment schedule

•PK parameters of CIT-013 by non-compartmental analysis of the serum concentration-time data after the single dose::

•AUCinf, AUClast, CL, Cmax, t1/2, tmax, Vz

•Dose-normalized PK parameters:

•AUCinf, AUClast, Cmax

Change from baseline to each time point of measurement during each treatment period:

• Circulating cytokines and/or chemokines induced by in vivo LPS challenge,

• Circulating immune cells induced by in vivo LPS challenge,

• Circulating NET components induced by in vivo LPS challenge

Part C

• Treatment-emergent (serious) adverse events ((S)AEs) throughout the study at every study visit, including frequency, duration and severity of local signs and symptoms at the injection site.

• Concomitant medication throughout the study at every study visit

• Vital signs (Pulse Rate (bpm), Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg)) as per assessment schedule

• Clinical laboratory tests (Haematology, blood chemistry and urinalysis) as per assessment schedule

• ECG parameters (Heart Rate (HR) (bpm), PR, QRS, QT, QTcB, QTcF) as per assessment schedule

• PK parameters of CIT-013 by non-compartmental analysis of the serum concentration-time data: Single ascending dose:

• AUCinf, AUClast, CL, Cmax, t1/2, tlag, tmax, Vz

• Dose-normalized PK parameters: AUCinf, AUClast, Cmax

Part D:

• Treatment-emergent (serious) adverse events ((S)AEs) throughout the study at every study visit, including frequency, duration and severity of local signs and symptoms at the injection site.

• Concomitant medication throughout the study at every study visit

• Vital signs (Pulse Rate (bpm), Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg)) as per assessment schedule

• Clinical laboratory tests (Haematology, blood chemistry and urinalysis) as per assessment schedule

• ECG parameters (Heart Rate (HR) (bpm), PR, QRS, QT, QTcB, QTcF) as per assessment schedule

PK parameters of CIT-013 by non-compartmental analysis of the serum concentration-time data after the first dose:

• AUCinf, AUClast, CL, Cmax, t1/2, tmax, Vz

• Dose-normalized PK parameters: AUCinf, AUClast, Cmax

PK parameters of CIT-013 by non-compartmental analysis of the serum concentration-time data after second dose:

• AUC0-14days, Cmax, t1/2, tmax

• Dose-normalized PK parameters: AUC0-14days, Cmax

Change from baseline to each time point of measurement during each treatment period:

• Circulating cytokines and/or chemokines,

• Circulating NET components

Study description

Background summary

Neutrophils, the most abundant type of leukocytes in human blood, contribute to the first line of defence and use their extensive armoury to protect the host against infection. Neutrophils kill microbes via phagocytosis, the generation of reactive oxygen species, or the release of their granular content. A more recently described antimicrobial function is the formation of neutrophil extracellular traps (NETs). NETs trap and efficiently eliminate pathogens and have been shown to protect mice and humans against bacterial and fungal infections. In spite of their importance in host defence, aberrant and prolonged NET release is associated with the pathophysiology of many acute and chronic inflammatory disorders. In particular, incomplete clearance of NETs contributes to vascular injury, which could lead to tissue damage and organ failure, or even death. NETs have been shown to block tissue repair signals, leading to impaired wound healing in diabetes, while activation of the clotting system by NETs occludes blood vessels in thrombosis. In addition, antimicrobial proteins and histones that are present in NETs are highly cytotoxic and induce endothelial dysfunction in systemic lupus erythematosus (SLE), vasculitis, and sepsis. Furthermore, NETs are a source of autoantigens and trigger autoimmunity, which is associated with the production of autoantibodies against various NET components in rheumatoid arthritis (RA), small-vessel vasculitis (SVV) antiphospholipid syndrome (APS) and SLE.

Several stimuli (e.g. microbes, cytokines, immune complexes) can initiate NET formation by binding to neutrophil receptors which activate the endoplasmic reticulum to release stored calcium ions. When this happens nuclear and granular membranes disintegrate, the chromatin decondenses and diffuses into the cytoplasm, where it mixes with cytoplasmic proteins. Citrullination of histones by protein arginine deiminase 4 (PAD4) as well as enzymatic degradation of nucleosomes by neutrophil elastase (NE) and Myeloperoxidase (MPO) enhances further chromatin decondensation. Finally, the cell-membrane breaks owing to the pressure exerted by the expanding chromatin, and the NET decorated with antimicrobial proteins and toxic histones is released into the extracellular space. Formed NETs are deposited in inflamed tissue but can also be found in the blood circulation during inflammation. Since the above-described process of NET formation is only happening in cases of microbial and sterile inflammation, it is near to absent in healthy individuals. If NETs appear in a healthy individual, they will readily be degraded by desoxyribonucleases. Citryll*s clinical development candidate CIT-013 is a first in class humanized monoclonal antibody, a so called therapeutic anti-citrullinated protein antibody (tACPA), that targets NET biology and its pathological effects. As a consequence, CIT-013*s targets (NETs containing citrullinated histones) are not present in healthy individuals. For this reason, in part B of the study, healthy volunteers are challenged with i.v. lipopolysaccharides (LPS) which causes a temporary inflammatory response and the induction of NETs. CIT-013*s effect on these inflammatory responses as

well as its NET inhibitory and clearance effect will be studied.

As NET formation is only initiated by either an acute stimulus (e.g. infection) or an aberrant chronic one (e.g. autoimmune or immune dysregulation), in part D of the study, Rheumatoid Arthritis (RA) patients with stable disease will be included to study CIT-013*s safety, tolerability and pharmacodynamics (effect on the inflammatory state, inhibition of NETs and consequences) and in particular CIT-013*s pharmacokinetics as this might differ from the pharmacokinetic profile in healthy volunteers due to target-mediated drug disposition effects.

Study objective

Objectives Part A:
• To evaluate the safety and tolerability of CIT-013 after administration of single, ascending, IV doses in healthy volunteers.
• To evaluate the pharmacokinetics of CIT-013 after administration of single, ascending, IV doses in healthy volunteers.

Objectives Part B:
• To evaluate the safety and tolerability of CIT-013 after administration of a single IV dose in LPS challenged healthy volunteers.
• To evaluate the pharmacokinetics of CIT-013 after administration of a single IV dose in LPS challenged healthy volunteers.
• To evaluate the pharmacodynamic effects of CIT-013 by characterizing the inflammatory response after administration of a single IV dose in LPS challenged healthy volunteers.

Objectives Part C:
• To evaluate the safety and tolerability of CIT-013 after administration of a single subcutaneous dose in healthy volunteers.
• To evaluate the bioavailability of CIT-013 after administration of a single subcutaneous dose in healthy volunteers.
• To evaluate the pharmacokinetics of CIT-013 after administration of a single subcutaneous dose in healthy volunteers.

Objectives Part D:
• To evaluate the safety and tolerability of CIT-013 after administration of two SC doses in patients with RA and healthy volunteers.
• To evaluate the pharmacokinetics of CIT-013 after administration of two SC doses in patients with RA and healthy volunteers.
• To evaluate the pharmacodynamic effects of CIT-013 by characterizing the inflammatory state and anti-inflammatory action of CIT-013 after administration of two SC doses in patients.

Study design

Part A is a double-blind, randomized, placebo controlled, single centre, single ascending dose study for the assessment of safety, tolerability and pharmacokinetic profiles of CIT-013 in healthy volunteers.

Part B is a double-blind, randomized, placebo controlled, single centre study of a single dose-level for the assessment of safety, tolerability, pharmacokinetic and pharmacodynamic profiles of CIT-013 in LPS challenged healthy volunteers.

Part C is a double-blind, randomized, placebo controlled, single centre study of two fixed dose-levels for the assessment of safety, tolerability, bioavailability and pharmacokinetic profiles of CIT-013 in healthy volunteers.

Part D is a double-blind, randomized, placebo controlled, single centre study of two SC doses for the assessment of safety, tolerability, pharmacokinetic and pharmacodynamic profiles of CIT-013 in RA patients and healthy volunteers.

Intervention

Part A
- Cohort 1: 0.1 mg/kg, 3 subjects CIT-013 / 3 subjects placebo
- Cohort 2: 0.3 mg/kg, 6 subjects CIT-013 / 2 subjects placebo
- Cohort 3: 0.9 mg/kg, 6 subjects CIT-013 / 2 subjects placebo
- Cohort 4: 0.9 mg/kg, 3 subjects CIT-013 / 1 subject placebo
- Cohort 5: 0.9 mg/kg, 3 subjects CIT-013 / 1 subject placebo
- Cohort 6: 3.0 mg/kg, 1 subject CIT-013 / 1 subject placebo
- Cohort 7: 1.8 mg/kg, 3 subjects CIT-013 / 2 subjects placebo

Part B
- Cohort 1a and 1b: dose dependent on data part A.
Up to 0.9 mg/kg, 3 subjects CIT-013 / 3 subjects placebo
- Cohort 2: dose dependent on data part A and data part B cohort 1.
Up to 3.0 mg/kg, 8 subjects CIT-013 / 6 subjects placebo.

Part C
- Cohort 1: 50 mg, 6 subjects CIT-013 / 2 subjects placebo
- Cohort 2: 100 mg, 6 subjects CIT-013 / 2 subjects placebo

Part D:
Cohort 1: two times 25 mg, 3 subjects CIT-013 / 2 subjects placebo
Cohort 2: two times 50 mg, 5 subjects CIT-013 / 1 subjects placebo

Placebo (NaCl 0,9%) infuuszakken zullen geblindeerd worden klaargemaakt en toegediend aan de proefpersonen voor deel A, B, cohort 1 van deel C.
Placebo (NaCl 2,0%) injecties worden bereid en geblindeerd toegediend aan de proefpersonen voor cohort 2 van deel C en deel D.

Placebo (NaCl 0.9%) infusion bags will be prepared and administered in a blinded manner to the subjects for part A, B and cohort 1 of part C.
Placebo (NaCl 2.0%) injections will be prepared and administered in a blinded manner to the subjects for cohort 2 of part C and part D.

Study burden and risks

Since the molecular target of CIT-013 (citrullinated histones) is not expressed in healthy volunteers, no on-target safety concerns apply for this healthy volunteer first-in-human study. Intravenous LPS challenges will be performed in study part B to drive the expression of CIT-013*s target. This allows the evaluation of the pharmacodynamic effect of CIT-013. Since the mechanism of action of CIT-013 is to stabilize and clear NETting neutrophils, exaggerated pharmacology is of no concern.
This will be the first administration of CIT-013 to humans, which will provide an initial assessment of the safety, pharmacokinetics and pharmacodynamics of CIT-013. Only healthy volunteers will participate, so study participants will not have any therapeutic benefit from participating in the planned study. Woman of childbearing potential will not be enrolled in the study. Safety precautions have been implemented in the clinical study protocol to potential risks to participating subjects.

In human whole blood cultures, CIT-013 drove IL-8 and TNFα responses at concentrations >=10 µg/mL, an exposure level regarded as *surrogate NOAEL*. IL-8 response size was comparable with Lemtrada, and the TNFα response size was a third of the response driven by Lemtrada. In a clinical setting, Lemtrada frequently gives cytokine induction after infusion (90%; at a dose of 12 mg giving a Cmax around 1 µg/mL). Based on the outcome of this experiment, caution should be paid for potential cytokine responses driven by CIT-013 in this clinical study. Dose escalations will be guided by cytokine levels observed in the preceding study cohort.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

lnclusion criteria part A- C, and HVs part D
Eligible subjects must meet all the following criteria at screening:
1. Healthy men or women, 18 to 55 years of age (inclusive) at screening. For part B cohort 2 only healthy men will
be included. The health status is verified by absence of evidence of any clinically significant activa or uncontrolled
chronic disease following a detailed medical history, a complete physical examination including vital signs,
laboratory measurements, and 12-lead ECG;
2. Signed infonmed consent, able and willing to comply wilh the requirements of the study protocol.
3. Body mass index (BMI) between 18 and 32 kg/m2, inclusive, and a body weight between 50 and 150 kg,
inclusive at screening.
4. All male and Women of Child Bearing Potenlial volunteers must practica effeclive contraception during the
study and be willing and able to continue contraception for at least 90 days after !heir last dose of study treatment.
5. Has the ability to communicate well with the lnvestigator in the Dutch language and willing to comply with the
study restriclions.

lnclusion criteria part D (patients)
Eligible subjects must meet all the following criteria at screening:
1. Men or women 18 to 75 years of age (inclusive) at screening diagnosed with RA (and fulfilling the ACR 2010 classification criteria for RA) for at least 6

months.
2. Signed informed consent, able and willing to comply with the requirements of the study protocol.
3. Body mass index (BMI) between 18 and 35 kg/m2, inclusive, and a body weight between 50 and 150 kg,
inclusive at screening.
4. All male and Women of Child Bearing Potential volunteers must practica effective contraception during the
study and be willing and able to continue contraception for at least 90 days after !heir last dose of study treatment.
5. Has the ability to communicate well with the lnvestigator in the Dutch language and willing to comply with the
study restrictions.
6. If on conventional DMARD, should be stable on a conventional DMARD (i.e. methotrexate, sulfasalazine, leflunomide and (hydroxy)chloroquine) (and steroids) for at least 8 weeks and willing to continue current stable treatment for 6 Weeks. Current treatment with
non-conventional DMARDs, including monoclonal antibodies, is not allowed. Prednisolone <= 10 mg / day is permitted.

Exclusion criteria

Exclusion criteria part A- C, and HVs in part D
Eligible subjects must not meet any of the following criteria at screening or pre-dose:
1. Evidence (following a detailed medical history, physical examination, vital signs, 12-lead ECG and clinical
laboratory parameters) of any active or chronic disease or condition that could interfere with, or for which the
treatment might interfere with, the conduct of the study, or that would pose an unacceptable risk to the subject in
the opinion of the investigator.
2. Clinically significant abnormalities, as judged by the investigator, in laboratory test results (including hepatic and
renal panels, complete blood count, chemistry panel and urinalysis). Minor deviations of laboratory values from the
normal range may be accepted, if judged by the lnvestigator or medically qualified designee as not clinically
significant. In the case of uncertain or questionable results, tests performed during screening may be repeated
before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects.
3. Any confirmed or suspected disease or condition associated with immune system impairment, including autoimmune
diseases, HIV, asplenia or recurrent severe infections.

4. Use of chronic (more than 14 days) immunosuppressant or immunomodulatory drugs within the 3 months prior
to IMP administration, or isolated (non-chronic) use within 30 days prior to IMP administration.
5. Any history of severe allergie reaction(s).
6. Any confirmed significant drug hypersensitivity reactions (including skin reactions or anaphylaxis), or known
allergies (non-active hay lever is acceptable).
7. Positive Hepatitis B surface antigen (HBsAg), Hepatitis C antibody (HCV Ab), or human immunodeficiency virus
antibody (HIV Ab) at screening, or other known infection requiring systemic antibiotic therapy within three months
prior to the study.
8. Subject has an active, uncontrolled acute or chronic systemic fungal, bacterial, and/or viral, infection within the
past 30 days.
9. Subjects with evidence or history of clinically significant haematological, renal, endocrine, pulmonary,
gastrointestinal, cardiovascular, hepatic, psychiatrie, neurologie diseases.
10. Subjects with a positive urine drug screen at screening or pre-dose.
11. Subject has a positive SARS-CoV-2 PCR based testwithin 72 hours prior to receiving CIT-013.
12. History of abuse of addictive substances (alcohol, illegal substances) or current use of more than 14 units
alcohol per week (in partAand B) and 14 units for females and 21 units lor males (in part C), drug abuse, or
regular user of sedatives, hypnotics, tranquillisers, or any other addictive agent.
13. Treatment with an investigational drug within 30 days or 5 half-lives (whichever is langer) preceding the first
dose of CIT-013.
14. Use of prescription or over-the-counter (OTC) drugs, vitamins, minerals and dietary supplements, within 7
days or 5 half-lives (whichever is langer) prior to the first dose of study medication until EOS. Herbal supplements
and hormone replacement therapy must be discontinued 30 days prior to the first dose of study medication until
EOS. Excluded from this list is paracetamol at doses of <4 g/day on all study days except day 1 of part B.
Exceptions will only be made il the rationale is clea~y documented by the investigator.
15. Receipt of live or attenuated vaccine 90 days prior to first study intervention administration.
16. Vaccination (completion of 2nd vaccination shot il applicable) against SARS-CoV-2 or influenza vaccinations
less than 14 days prior to first study drug administration.
17. Known hypersensitivity to any of the constituents or excipients of CIT-013

or history of relevant drug and/or
food allergy (anaphylactic, anaphylactoid reactions).
18. Excessive caffeine consumption, defined as >800 mg per day from 7 days prior to the first dose of the study
drug until 24 hours prior to dosing. Subjects will abstain from
caffeine-containing products lor 24 hours prior to the
start of dosing until discharge trom the study unit. Caffeine quantities
defined as: one cup of coffee contains 100
mg of caffeine; one cup of tea, or one glass of cola, or portion of chocolate (dark:100 g, milk 200 g) contains
approximately 40 mg of caffeine; one bottle of Red Bull contains approximately 80 mg of caffeine.
19. Donation (or loss) of whole bloed or plasma of 500 ml or more du ring the 12 weeks prior to CIT-013
administration.
20. Smoking > than 10 cigarettes (or equivalent) per week and/or using nicotine-based products within 1 month
prior to CIT-013 administration and/or unwillingness to abstain trom the use of these trom screening until EOS.
21. Any ether known factor, condition, or disease that, in the opinion of the lnvestigator, might interfere with
treatment compliance, study conduct or interpretation of the results, or may compromise volunteer safety.
22. Extreme exercise (e.g. marathon or triathlon) within 2 weeks of screening (part A and B) and extreme exercise
(e.g. marathon or triathlon) within 2 weeks of screening or admission (part C).
23. Subject has participated in an intraveneus LPS challenge study before (Part B only).

Exclusion criteria part D (patients)
Eligible subjects must not meet any of the following criteria at screening or pre-dose:
1. Evidence (following a detailed medical history, physical examination, vital signs, 12-lead ECG and clinical
laboratory parameters) of any active or chronic disease or condition ether than Rheumatoid Arthritis that could
interfere with, or lor which the treatment might interfere with, the conduct of the study, or that would pose an
unacceptable risk to the subject in the opinion of the investigator.
2. Clinically significant abnormalities, as judged by the investigator, in laboratory test results (including hepatic and
renal panels, complete bloed count, chemistry panel and urinalysis) not associated with Rheumatoid Arthritis,
known comorbidity or the use of concomitant medication. Minor deviations of laboratory values from the normal
range may be accepted, il judged by the lnvestigator or medically qualified designee as not clinically significant. In

the case of uncertain or questionable results, tests performed during screening may be repeated before
randomization to confirm eligibility or judged to be clinically irrelevant for the patient.
3. Any confirmed or suspected disease or condition other than Rheumatoid Arthritis, associated with immune
system impairment, including auto-immune diseases, HIV, asplenia or recurrent severe infections. Any confirmed
significant drug hypersensitivity reactions (including anaphylaxis), or known allergies (non-active hay fever is
acceptable).
4. Any confirmed significant drug hypersensitivity reactions (including anaphylaxis), or known significant allergies (non-active hay fever, cat/dog allergies or very mild non-relevant reactions are acceptable).
5. Positive Hepatitis B surface antigen (HBsAg), Hepatitis C antibody (HCV Ab), or human immunodeficiency virus
antibody (HIV Ab) at screening, or other known infection requiring systemic antibiotic therapy within three months
prior to the study.
6. Subject has an active, uncontrolled acute or chronic systemic fungal, bacterial, and/or viral, infection within the
past 30 days.
7. Subjects with a positive urine drug screen at screening or pre-dose.
8. Subject has a positive SARS-CoV-2 PCR based test within 72 hours of receiving CIT-013.
9. History of abuse of addictive substances (alcohol, illegal substances) or current use of more than 14 units
alcohol per week, drug abuse, or regular user of sedatives, hypnotics, tranquillisers, or any other addictive agent.
Exceptions will only be made if the rationale is clea~y documented by the investigator.
10. Treatment with an investigational drug within 30 days or 5 half-lives (whichever is longer) preceding the first
dose of CIT-01

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	28-07-2021
Enrollment:	84
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	CIT-013
Generic name:	NA

Ethics review

Approved WMO Date:	27-05-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-07-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-08-2021
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-11-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	12-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	29-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-09-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-09-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-12-2023

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-01-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-01-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-04-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-05-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-05-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 24009
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2020-005848-36-NL
CCMO	NL77528.056.21