# A PHASE II, RANDOMISED, ADAPTIVE, OPEN-LABEL PLATFORM TRIAL TO EVALUATE EFFICACY AND SAFETY OF MULTIPLE COMBINATION THERAPIES IN PARTICIPANTS WITH CHRONIC HEPATITIS B

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Primary* To estimate the effect of NME combination therapies on inducing a functional cure over the control arm.Secondary * To characterize the efficacy profile of NME combination therapies.* To characterize the PD profile of NME combination…

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Will not start |
| **Health condition type** | Viral infectious disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON50813

**Source**
ToetsingOnline

**Brief title**
COMBINATION THERAPIES FOR CHB

### Condition

- Viral infectious disorders

**Synonym**
chronic disease, viral infection

**Research involving**
Human

## Sponsors and support

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

## Intervention

**Keyword:** Chronic Hepatitis B, Open-label, Phase II, Randomized

## Outcome measures

### Primary outcome

Primary Endpoint

* % participants with HBsAg loss at 24 weeks post-EOT.

### Secondary outcome

Secondary Endpoint

* % participants with HBsAg loss

* % participants with HBsAg seroconversion.

* % participants with HBeAg loss (baseline HBeAg-positive participants).

* % participants with HBeAg seroconversion (baseline HBeAg-positive participants).

* % participants with HBV DNA < lower limit of quantification (LLOQ), <200 IU/mL and <2,000 IU/mL.

* Including but not limited to: change from baseline in quantitative HBsAg, anti-HBs, HBeAg, anti-HBe, anti-HBc, HBcrAg, HBV RNA, and HBV DNA levels over time.

* Estimated PK parameters from sparse sampling and population PK models.

* Incidence, nature, and severity of AEs and laboratory abnormalities.

* Analyses of PK/PD data.

* Relationship between ADA status, PK, safety, PD, and efficacy

# Study description

**Background summary**

Chronic HBV infection (defined as persistent detection of serum HBsAg, the hallmarks of which are high levels of circulating HBV DNA and HBsAg) is a consequence of the presence of a viral reservoir, i.e., episomal covalently closed circular deoxyribonucleic acid (cccDNA) in the nucleus of an infected hepatocyte. Despite advancements in the understanding of HBV disease biology, complete cure, i.e., eradication of cccDNA is not
currently possible by available treatments. Nevertheless, the sustained clearance of HBsAg has been shown to protect against disease progression and development of HBV complications including cirrhosis, liver failure, and HCC. Accordingly, functional cure is defined as sustained, undetectable HBsAg in serum and HBV DNA in circulation, with or without seroconversion to anti-HBs, after completion of a finite course of treatment
(Lok et al 2017). Partial cure will demonstrate sustained plasma HBV DNA suppression after completion of treatment, but with persistently detectable circulating HBsAg.
Other clinically meaningful endpoints include HBV DNA suppression and alanine aminotransferase (ALT) normalization, which indicate virologic and biochemical responses to therapies, respectively. For hepatitis B e antigen (HBeAg)-positive patients,HBeAg seroconversion is indicative of a better prognosis, including lower rates of cirrhosis and slower disease progression. Sustained suppression of HBV replication,
regardless of HBeAg status, is associated with biochemical remission, histological improvement, and reduced risk of disease progression.

**Study objective**

Primary
* To estimate the effect of NME combination therapies on inducing a functional cure over the control arm.

Secondary
* To characterize the efficacy profile of NME combination therapies.

* To characterize the PD profile of NME combination therapies.
* To characterize the plasma PK profiles of NMEs.
* To assess the safety and tolerability of NME combination therapies.
* To identify presence of PK/PD relationship.
* To explore potential effects of ADA on NMEs and/or IMP, as applicable.

**Study design**

This is a Phase II, randomized, adaptive, open-label, multi-arm, multi-center, international, platform study designed to evaluate safety, tolerability, and efficacy of new combination therapies including one or more NMEs in CHB participants with preserved liver function and without significant fibrosis/cirrhosis. The platform design allows comparison of multiple new combination therapies against a common control, and introduction of additional treatment arms at later study time points.

This study is designed to be adaptive to open additional shorter duration treatment arms or to expand existing treatment arms for NME combination therapies that show promising efficacy outcomes. The platform design also has the flexibility to open new treatment arms to explore different combination regimens or different patient populations pending new submission and HA/EC approval. Treatment arms may be staggered relative to other treatment arms in order to increase study efficiency with regards to timely interim data readouts or to reduce the complexity of study conduct.
For the first combination, participants will be randomized on Day 1 to an NME combination arm (N=30) or the control arm (N=30) using an adaptive stratified sampling method, stratified at screening HBsAg level (* 1,000 IU/mL, * 1000 IU/mL), with a minimum of 12 participants per arm with a screening HBsAg level of * 1000 IU/mL. For NME combination arms that will be introduced later into the platform study, the allocation ratio of participants to the control arm, will depend on the number of actively enrolling arms with the stipulation that no more than 17% of participants will be randomly allocated to a control arm. Additionally, for subsequent arms the proportion of patients with HBsAg level * 1000 IU/mL, * 1000 IU/mL within each treatment arm, will be maintained as closely as possible to the first combination treatment arm.

The treatment period duration will be a maximum of 48 weeks, after which participants will enter a 48-week follow-up period. A shorter treatment duration (12 or 24 weeks) for NME combination arms, and a 48-week response-guided therapy (RGT) arm may be added following planned interim analyses; four interim analyses are planned for each treatment arm. Treatment arms that achieve 30% difference, compared to NUC control arm, for HBsAg loss at EOT or follow-up Weeks 12 and 24 (primary endpoint) may be expanded to accrue additional efficacy and safety data and to contribute to Phase 3 design planning as guided by the emerging data, for example, enrichment for HBeAg positive or HBeAg negative participant populations.

**Intervention**

Screening
* Physical examination
* Vital Signs
* Electrocardiogram (ECG)
* Abdominal ultrasound scan
* Liver elastography
* Blood collection
* Urine samples
* Breath test: A breath test to test for alcohol consumption.
These tests may be repeated or extra samples may be collected if the laboratory results fall outside of the required ranges.

NUC Control arm
* Physical examination:
* Vital Signs:
* Electrocardiogram (ECG)
* Abdominal ultrasound scan:
* Blood collection
* Urine samples
* Breath test:
These tests may be repeated or extra samples may be collected if the laboratory results fall outside of the required ranges, or if the patient has a reaction to the study medications.

siRNA + NUC arm
* Physical examination:
* Vital Signs
* Electrocardiogram (ECG)
* Ultrasound
* Blood collection
* Urine samples
* Breath test
These tests may be repeated or extra samples may be collected if the laboratory results fall outside of the required ranges, or if the patient has a reaction to the study medications.

siRNA + PEG-IFN + NUC arm
* Physical examination:
* Vital Signs
* Electrocardiogram (ECG)
* Abdominal ultrasound scan
* Blood collection
* Urine samples
* Breath test

These tests may be repeated or extra samples may be collected if the laboratory results fall outside of the required ranges, or if the patient has a reaction to the study medications.

siRNA + TRL7 + NUC arm
* Physical examination:
* Vital Signs
* Electrocardiogram (ECG)
* Abdominal ultrasound scan
* Blood collection
* Urine samples
* Breath test
These tests may be repeated or extra samples may be collected if the laboratory results fall outside of the required ranges, or if the patient has a reaction to the study medications.

**Study burden and risks**

There is no guarantee that the patient will receive any benefits from this study, and taking part in this study may or may not cause patient's health to improve. Information from this study may help doctors learn more about the investigation combination treatments and the treatment of chronic HBV infection. This information may benefit other patients with chronic HBV infection or a similar condition in the future.

Disadvantages of participation in the study may be:
- possible side effects of the study drug
- possible discomforts from the measurements during the study
- (additional) testing
- appointments that need to be attended
- possibly confrontational questionnaires

Patients may have side effects from the medications or procedures used in this study. Side effects can vary from mild to serious and may vary from person to person. Some side effects go away soon after patients stop the medication that is causing them. In some cases, side effects can be serious (in very rare cases may be fatal) and may be long lasting or may never go away. Patients should talk to the study doctor about any side effects that they have while taking part in the study. Everyone taking part in the study will be monitored carefully for any side effects, and cared for as appropriate. Study doctors may give patients medications to help lessen any side effects.

Allergic reactions can occur with any medication and this can be in the form of itching, difficulty breathing, and a skin rash and/or drop in blood pressure. In very rare cases, patients could suffer a life-threatening allergic reaction.

Side Effects Potentially Associated with NUCs and PEG-IFN

NUCs and PEG-IFN have been used for many years to treat chronic HBV infection.
* For entecavir: https://packageinserts.bms.com/ppi/ppi_baraclude.pdf
The most common side effects of entecavir are headache, feeling tired, dizziness, nausea, and elevated liver enzyme (ALT). Patients with HBV may experience worsening of their liver disease if entecavir treatment is stopped prematurely.
* For tenofovir alafenamide (TAF): https://www.vemlidy.com/isi
In patients with HBV treated with TAF, the most common side effects (greater than 10% of subjects) was headache. Patients with HBV may experience worsening of their liver disease if TAF treatment is stopped prematurely. TAF may also impair kidney function.
* For tenofovir disoproxil fumarate (TDF):

http://www.gilead.com/~/media/Files/pdfs/medicines/hiv/viread/viread_patient_pi.pdf
In patients with HBV treated with TDF, the most frequently reported side effects were nausea (9%), abdominal pain (>5%), diarrhea (>5%), headache (>5%), dizziness (>5%), fatigue (>5%), nasopharyngitis (common cold) (>5%), back pain (>5%), and skin rash (>5%). Patients with HBV may experience worsening of their liver disease if TDF treatment is stopped prematurely. TDF may also impair kidney function.
* For pegylated interferon alfa-2a (PEG-IFN):
https://www.medicines.org.uk/emc/files/pil.1697.pdf
In HBV patients treated with PEG-IFN, the most common side effects were pyrexia (54%), headache (27%), fatigue (24%), myalgia (26%), alopecia (18%), and anorexia (16%). Overall 5% of HBV subjects discontinued PEG-IFN therapy and 40% of subjects required modification of PEG-IFN dose. The most common reason for dose modification in subjects receiving PEG-IFN therapy was for laboratory abnormalities including neutropenia (20%), thrombocytopenia (13%), and liver enzyme (ALT) elevation (11%).

Side Effects Potentially Associated with RO7445482
Therapies such as RO7445482, which are called oligonucleotides, may be associated with certain side effects (called class effect) in animals or humans. Known oligonucleotide class effects may affect the kidneys (the organ where the drug is eliminated), the liver (the organ where the drug is metabolized/broken down), the skin (at the sites where the drug is administered), or trigger immune reactions (such as flu-like symptoms, or antibodies against the drug). RO7445482 is an experimental drug with limited clinical experience in humans. For this reason, the side effects are not known at this time. There is one clinical study with RO7445482, (DCR-HBVs-101) that is currently ongoing. By the 25th of June 2020, 30 healthy volunteers, 9 patients with HBV who had not previously been treated with standard therapy and 18 patients with chronic HBV who were being treated with NUCs had received RO7445482 or placebo (a substance that looks like RO7445482, but has no medication). RO70445482 was generally well tolerated, the majority of the side effects were mild in nature, and most had resolved. The healthy volunteers

received single doses of RO7445482 or placebo and the most frequently reported side effects were reactions at the injection site, headaches, abdominal pain, dizziness, and vomiting. The patients with HBV received single or multiple dose of RO7445482 or placebo and the most frequent side effects reported were injection site reactions (ISRs), increases in liver enzymes (ALT, AST and GGT), headache, and fatigue.

Injection Site Reactions and Risks Associated with Drug Administration
For SC administration, the study drug will be given through a syringe into the skin layer in the abdomen or thigh. Patient may experience mild discomfort during the procedure, and there is a small chance of infection or bruising by placing the needle in the abdomen/thigh (subcutaneously).
ISRs could occur at the time of RO7445482 administration, within 24 hours after administration, or even later. Most of the ISRs were considered mild in intensity. Most common symptoms generally reported in the ongoing clinical study were redness, rash, local swelling, discoloration, and pain or tenderness at the injection site. Study doctor will be carefully assessing the injection site and every medical precaution will be taken to avoid an infection or complication.

Liver Effects
In animal studies (in mice), some changes in liver enzyme laboratory tests were observed, however, no liver safety signals were observed in monkeys (monkey is considered the most relevant animal for assessing the risk to humans). Study doctor will carry out safety laboratory tests to monitor patien's liver and avoid any complications. Transient elevations in liver enzymes were observed in patients with HBV who had not previously been treated with standard therapy in the ongoing clinical trial between 2 to 4 weeks after receiving RO7445482, which resolved during the follow-up period without the need of treatment.

Other Potential Oligonucleotide Class Effects
To date, studies in animals (mice and monkeys) showed that RO7445482 was not associated with any changes in kidney functions. In the ongoing studies, no drug-related kidney side effects, changes in kidney laboratory parameters, or abnormalities in urine microscopy were reported. Study doctor will carry out safety laboratory tests to monitor your kidney to avoid any complications.
Based on information from animal studies and other similar drugs, RO7445482 is considered of low risk to trigger immune reactions (meaning, reactions of the system in the body that fights infections). Study doctor will monitor the patient for any immediate reactions after the administration of the study drug. All participants will be closely monitored.

Unknown Risks:
RO7445482 might have other side effects, including serious side effects, that could occur with long-term treatment or when used in combination, which are not known at this time. Such side effects cannot always be predicted. If new information is discovered that might change patient's decision to stay in the

study, the patient will be told about it in due time, so the patient can decide whether he/she want to continue.

Side Effects Potentially Associated with RO7020531
RO7020531 is an experimental medication that, as of 01 May 2020, had been administered to 88 healthy volunteers, 24 HBV patients, and to 56 Chinese healthy volunteers in two clinical studies, one of which is currently ongoing. Patient will be informed about any additional side effects that may occur in this ongoing study. The study medication was considered safe and with acceptable tolerability in the majority of patients. Nineteen (out of 72) subjects who received multiple doses of RO7020531 at 140 mg or higher experienced flu-like symptoms (such as fever, body ache, headache, chills, dizziness, and nausea). In some subjects, flu-like symptoms may re-appear with the subsequent dosing. However, these symptoms are commonly resolved with treatment to reduce fever (e.g. paracetamol). Some subjects with flu-like symptoms may also experience a temporary decline in their blood cells count, but these cells return to normal within 24-48 hours after dosing. Since RO7020531 causes the activation of patient's immune system, the body will produce some molecules (called cytokines) that include interferon-*. A modified version of interferon-* is currently used as treatment for HBV. Even though RO7020531 induces lower levels of interferon-* and will be given for shorter duration, there is the potential to cause a similar spectrum of side effects, which patient may find here:
https://www.medicines.org.uk/emc/files/pil.8244.pdf
In rare cases, there is a potential for medications with a similar mechanism of action of RO7020531 to cause an excessive activation of patient's immune system (an extreme form of flu-like symptoms including fever). This may cause a potentially life-threatening condition that can lead to blood pressure drop and toxicity to patient's organs which requires hospitalization. RO7020531 has been given to 168 healthy volunteers/HBV patients, 96 of which received doses equal to or higher than 140 mg, similar to the dose to be used for this study (150 mg) and no participant experienced this condition.

Risks Associated with Study Procedures
- Blood Sampling
During this study, small amounts of blood will be drawn from a vein and used for tests that allow study doctors to see how the patients are doing. Drawing blood may cause pain where the needle is inserted, and there is a small risk of bruising or infection at the place where the needle is inserted. Very rarely, a blockage of the vein or a small nerve injury can occur, resulting in numbness and pain. However, this will resolve with time. Some people experience dizziness, upset stomach, or fainting when their blood is drawn. On days when several blood samples will be taken, the study nurse may use a cannula (small plastic tube) inserted in patient's arm using a small needle. This cannula may remain in place for the day and will be taken out before patients go to bed at night. There is a small chance of infection by placing the cannula in the arm, but every medical precaution will be taken to avoid an infection.

- Electrocardiogram (ECG)
Patients will have small, soft pads, placed stuck temporarily on different parts of their body. There is no pain or discomfort during an ECG; however, the area of skin in which the ECG pads will be stuck may need to be shaved, and the pads may cause a skin reaction such as redness or itching. Taking the pads off may cause localized irritation to the skin and/or hair loss, similar to having a plaster taken off.
- Liver biopsy
In case patients experience any marked and persistent liver enzyme (ALT) elevations, study doctor may suggest to perform a liver biopsy, if this procedure is considered a relevant assessment for patient's clinical condition. If a liver biopsy is to be done, then patients may need to stay in the hospital for several hours. The procedure includes numbing the skin over the liver with a local anesthetic, followed by passing a needle through the skin into the liver and removing a small core of liver tissue. A specialist will examine the tissue carefully under a microscope. There is some discomfort associated with the procedure. The discomfort should generally not last more than several hours. The risks include bleeding from the biopsy site, significant bleeding requiring a blood transfusion or surgery to control the bleeding (rare), perforation of internal organs (rare), and death (very rare).

# Contacts

**Public**
Covance

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**Scientific**
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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)

## Inclusion criteria

Informed Consent
1. Able and willing to provide written informed consent and to comply with the study
protocol according to International Council for Harmonization (ICH) and local regulations.
Age
2. Participants must be between 18 and 65 years of age, inclusive, at the time of
signing the informed consent.
Weight
3. Body mass index between 18 and 32 kg/m2 inclusive.
Type of Participants and Disease Characteristics
4. Participants with CHB infection (HBsAg positive for **6 months) who are on NUC
(entecavir or tenofovir alafenamide/disoproxil fumarate) monotherapy
for *12 months, having received the same NUC therapy for** 3 months prior to screening.
5. HBV DNA below the LLOQ or < 20 IU/mL for > 6 months prior to screening and confirmed at screening.
6. Alanine transaminase (ALT) **1.5 x upper limit of normal (ULN) for > 6 months prior
to screening, and confirmed at screening
7. Screening laboratory values (hematology, chemistry, urinalysis) within normal range, or judged not clinically significant by the Investigator and Medical Monitor.
Sex
8. Male and female participants:
The contraception and abstinence requirements are intended to prevent exposure of
an embryo to the study treatment. The reliability of sexual abstinence for enrollment
eligibility needs to be evaluated in relation to the duration of the clinical study and
the preferred and usual lifestyle of the participant. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or post-ovulation methods) and withdrawal are
not acceptable methods of preventing fetal/embryonic drug exposure.
The following contraception requirements must be followed unless otherwise

stated
in the respective appendix of each treatment arm.
a) Female Participants:
A female participant is eligible to participate if she is not pregnant (see Appendix 5),
not breastfeeding, and at least one of the following conditions applies:
* Woman of non-childbearing potential (WONCBP), as defined in Appendix 5.
* Woman of childbearing potential (WOCBP), who:
* Agrees to remain abstinent (refrain from heterosexual intercourse) or use highly effective contraceptive methods that result in a failure rate of <1% per year during the treatment period and for at least 6 months after the final dose of
study treatment. Examples of contraceptive methods with a failure rate of <1% per year include bilateral tubal occlusion, male sterilization, established proper
use of hormonal contraceptives that inhibit ovulation, hormone-releasing intrauterine devices, and copper intrauterine devices (see Appendix 5).
* Has a negative pregnancy test at screening (Day -14 to -7). In addition, WOCBP must be willing to undergo a urine pregnancy test every 3 months until the end of
study.
b) Male Participants:
During the treatment period and for at least 6 months after the final dose of study
treatment, agree to:
* Remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures such as a condom plus an additional contraceptive method that together result in a failure rate of <1% per year, with a partner who is a woman of childbearing potential (WOCBP, as defined in Section 1 in Appendix 5).
* With pregnant female partner, remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures such as a condom to avoid exposing the embryo.
* Refrain from donating sperm.

## Exclusion criteria

Medical Conditions
1. Pregnant (positive pregnancy test) or lactating women.
2. Co-infection with other pathogens such as hepatitis A (HAV), hepatitis C (HCV),
hepatitis D (HDV), hepatitis E (HEV), or human immunodeficiency virus (HIV).
3. History of cirrhosis or current evidence of significant liver fibrosis or cirrhosis (F3 or
above on liver biopsy, *7.4 kPa on transient elastography, >1.32 m/s on acoustic

radiation force impulse [ARFI] elastography, or >3.13 kPa on magnetic resonance [MR]
elastography), or decompensated liver disease (e.g., ascites, hepatic encephalopathy). Liver biopsy or transient elastography/ARFI/MR result must be obtained within 6 months prior to randomization.
4. History of or suspicion of hepatocellular carcinoma (HCC) (e.g, elevated *-fetoprotein
[AFP] levels, suggestive lesions on abdominal ultrasound or other imaging, etc.).
5. Thyroid disease poorly controlled on prescribed medications or clinically relevant
abnormal thyroid function tests (thyroid-stimulating hormone [TSH], free triiodothyronine [FT3], free thyroxin [FT4]) at screening, as judged by the Investigator and Medical Monitor.
6. Clinically significant disease other than CHB that, in the opinion of the Investigator,
makes the participant unsuitable for the study.
7. Pre-existing cardiac disease that in the opinion of the investigator would increase
the risk for the patient to participate to the study.
8. History of alcohol abuse and/or drug abuse within one year of randomization.
9. History of having received (in the last 6 months) or currently receiving any systemic antineoplastic
(including radiation) or immunosuppressive (including biologic immunosuppressors) or immune modulating treatment (including non-biological oral immune modulating drugs; e.g., methotrexate > 25 mg per week, azathioprine > 3.0 mg/kg/day or 6-mercaptopurine > 1.5 mg/kg/day) for malignant or
non-malignant disorders.
10. Currently taking, or have received within 3 months of Day 1, systemic corticosteroids at a
high-dose (e.g., 40 mg prednisolone per day for) > 7 days, or a low-dose (e.g., 20 mg
prednisolone per day) for > 14 days.
Diagnostic Assessments
11. Electrocardiogram (ECG) with clinically significant abnormalities, including QTcF
interval (QT corrected using Fridericia*s formula) *450 msec for males and *470 msec for females at screening.
12. Laboratory parameters at screening:
a) Hemoglobin <12 g/dL (females) or <13 g/dL (males); platelets normal (LLN); international normalized ratio (INR) >1.1.
b) Albumin <3 g/dL; total bilirubin >ULN (exception: Gilbert*s disease).
c) Positive results for anti-mitochondrial antibodies (AMA >1:80), antinuclear antibody (ANA >1:80), anti*smooth muscle antibody (ASMA >1:40), or antithyroperoxidase
antibodies (a-TPO >10).

d) White blood cell count <2500 cells/mm3; neutrophil count <1500 cells/mm3 (<1000 cells/mm3 if considered a physiological variant in a participant of African
descent).
e) Glomerular filtration rate (GFR; using Modification of Diet in Renal Disease [MDRD]) * 60 mL/min.
f) Positive test for drugs of abuse (including recreational drugs) and/or positive alcohol
test at screening. For positive cannabinoids test, the eligibility is at the Investigator*s
discretion.
Prior/Concurrent Clinical Study Experience
13. Previous treatment with an investigational agent for HBV within 6 months prior to
screening.
14. Unable to comply with any drugs or nutrients listed in prohibited medications and
prohibited food sections in the respective treatment arm appendix.

# Study design

## Design

| | |
|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Other |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Will not start |
| Enrollment: | 6 |
| Type: | Anticipated |

### Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | PEG-IFN |
| Generic name: | Pegasys 180 mg solution for injections in pre-filled syringe |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | RO7020531 |

## Ethics review

| | |
|---|---|
| Approved WMO Date: | 11-03-2021 |
| Application type: | First submission |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 27-09-2021 |
| Application type: | Amendment |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 25-10-2021 |
| Application type: | Amendment |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 05-11-2021 |
| Application type: | First submission |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO Date: | 19-11-2021 |
| Application type: | Amendment |
| Review commission: | CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag) |
| Approved WMO | |

| | |
|---|---|
| Date: | 01-12-2021 |
| 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 | EUCTR2019-002086-35-NL |
| ClinicalTrials.gov | NCT04225715 |
| CCMO | NL76220.000.21 |