# A Three-Part, Single-Arm, Open-Label Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Evinacumab in Pediatric Patients with Homozygous Familial Hypercholesterolemia

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PrimaryThe primary objective for Part A of the study is to assess the pharmacokinetics (PK) of evinacumab in pediatric patients with homozygous familial hypercholesterolemia (HoFH).The primary objective for Part B of the study is to demonstrate a...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Lipid metabolism disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON52413

**Source**
ToetsingOnline

**Brief title**
R1500-CL-17100 (0456/0292)

### Condition

- Lipid metabolism disorders

**Synonym**
hereditary abnormal high cholesterol level, homozygous familial hypercholesterolemia

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Regeneron Pharmaceuticals, Inc.,
**Source(s) of monetary or material Support:** the study sponsor as listed in B7

## Intervention

**Keyword:** evinacumab (REG1500), Homozygous Familial Hypercholesterolemia (HoFH), pediatric patients, phase 1b/3

## Outcome measures

### Primary outcome

The primary endpoint for Part A is the PK parameters for evinacumab, including

Cmax, AUC, and linear t* following a single administration of evinacumab.

The primary endpoint for Part B is the percent change in calculated LDL-C from

baseline to week 24 (intent-to-treat [ITT] estimand) in Part B. The primary

endpoint is defined as: 100x (calculated LDL-C value at week 24 - calculated

LDL-C value at baseline)/calculated LDL-C value at baseline.

### Secondary outcome

The secondary endpoint for Part A is:

• Incidence of treatment-emergent adverse events (TEAE) and other safety

variables over time

The secondary endpoints in Part B are:

• The percent change in Apo B from baseline to week 24 (ITT estimand)

• The percent change in non-HDL-C from baseline to week 24 (ITT estimand)

• The percent change in total cholesterol (TC) from baseline to week 24 (ITT

estimand)

• The proportion of patients with >=50% reduction in calculated LDL-C at week 24

(ITT estimand)

• The percent change in calculated LDL-C from baseline to week 24 in patients

who have negative/negative and null/null mutations (ITT estimand)

• The percent change in lipoprotein a [Lp(a)] from baseline to week 24 (ITT

estimand)

• The absolute change in LDL-C at week 24 (ITT estimand)

• Incidence of treatment-emergent adverse events (TEAE) and other safety

variables over time

• Concentrations of total evinacumab over time

• Incidence and titer of treatment-emergent anti-drug antibodies over time

# Study description

**Background summary**

Familial hypercholesterolemia (FH), a primary hyperlipidemia driven by genetic mutation(s) primarily in the low-density lipoprotein (LDL) receptor (LDLR), is the most common monogenic hypercholesterolemia condition in children. The most rare and severe form of FH is homozygous familial hypercholesterolemia (HoFH). It is an inherited autosomal dominant disorder primarily resulting from mutations in the LDLR or, less frequently, from mutations in 3 associated genes: proprotein convertase subtilisin/kexin type 9 (PCSK9), apolipoprotein B (APOB), and LDL receptor adaptor protein 1 (LDLRAP1). Depending on the genes affected and the mutations that are present, patients are categorized as either true homozygotes, compound heterozygotes, or double heterozygotes. True homozygotes have the same mutation on both alleles. Compound heterozygotes have different mutations on the 2 alleles. Double heterozygotes have mutations in 2 different genes. The resulting phenotype includes deficient or defective LDL receptors on the surface of hepatocytes causing impaired clearance of circulating low-density lipoprotein cholesterol (LDL-C). This leads to severe hypercholesterolemia, often 3 to 6 times normal (>=500 mg/dL), starting in infancy, which results in an exceedingly high risk of developing premature atherosclerosis, as well as valvular and supravalvular stenosis.
The etiology of the hypercholesterolemia observed in patients with HoFH is the same for both adult and pediatric patients. It is a consequence of the above

mentioned abnormal lipoprotein metabolism due to mutations in the key genes listed above, and the markedly diminished hepatic LDL-C clearance from plasma (Goldstein, 2001)(Kolansky, 2008)(Macchiaiolo, 2012) (Rader, 2003). These high plasma levels lead to vascular damage starting from birth and morphological and functional vascular changes by 8 years of age or earlier. Children as young as 7 years of age can present with coronary atherosclerosis even without any clinically apparent coronary artery disease. This accelerated atherosclerosis results in premature cardiovascular disease (CVD) and an increased risk of CV events at a young age. Evidence of accelerated atherosclerosis include children with increased carotid intima-media thickness (cIMT) and cIMT progression at a rate approximately double that of unaffected siblings. An observational study of HoFH patients showed that the mean age for first major CV event was 20 years (Goldstein, 2001)(Kolansky, 2008)(Macchiaiolo, 2012)(Rader, 2003). Indeed, if left untreated, children and adolescents with HoFH, have an extremely high risk for premature CVD and reduced life expectancy. For example, in a longitudinal study of 39 pediatric patients with HoFH followed for up to 8 years, 88% of patients >16 years of age and 9% <16 years of age developed CVD. Further, during follow-up, 7 patients developed progression of coronary and/or aortic valvular disease and 4 required surgical intervention (Kolansky, 2008), demonstrating the need for early aggressive lipid-lowering therapy in pediatric subjects with HoFH.

The frequency of HoFH in the general population is historically reported as 1/1,000,000. This estimate is based on a heterozygous familial hypercholesterolemia (HeFH) prevalence of 1/500 and the application of the Hardy-Weinberg equilibrium (1/1,000,000 = 1/500 mother * 1/500 father * 1/4 risk for child). However, based on more recent data, HoFH has an estimated prevalence of 1/300,000, which would be the same in children. Populations with a founder effect have higher prevalence rates.

Diagnosis of HoFH can be made based on clinical criteria or genetic criteria (Section 7.2.1 ). An LDL-C level >=13 mmol/L (>=500 mg/dL) is consistent with phenotypic HoFH. However, the LDL-C criteria could be lower depending on the presence of positive family history and age of screening. Additional phenotypic characteristics include premature coronary heart disease, aortic valve disease, and tendon xanthomas in the hands and Achilles tendons. Clinically identified patients could undergo genetic testing to confirm diagnosis.

Patients with HoFH can be further classified based on the phenotype of the LDLR mutation(s), ranging from defective mutations (where the LDLR retains some LDL-binding functionality) to null or negative mutations where no functioning LDLR is expressed. Patients who have LDLR activity <15% are considered null and patients whose LDLR activity is impaired but >15% are LDLR defective (Banerjee, 2019). Another method that could be used to categorize these mutations is to define a negative mutation status as having mutations in stop codons, frame shifts, splice site changes, small and large insertions/deletions, and copy number variations (CNVs) predicted to result in the loss of function of the LDLR. The most extreme cases are those patients who are LDL-receptor negative or null in both alleles. These patients tend to have LDL-C levels at the highest end of the range and experience very little efficacy from existing

therapies such as statins and PCSK9 inhibitors. As such, significantly accelerated atherosclerosis and worse clinical outcomes are observed in these patients compared to those who are LDLR defective (Kolansky, 2008) (Moorjani, 1993). Patients who are LDLR null or negative develop xanthomas sooner than patients who are LDLR receptor defective, and untreated patients who are LDLR null or negative rarely live past the second decade of life (Kolansky, 2008) (Moorjani, 1993).

Current approved therapies for patients with HoFH include statins, lomitapide, ezetimibe, evolocumab, and lipoprotein apheresis. All but lomitapide are approved for use in pediatric patients >=12 years of age. Some of the statins are approved in younger patients (rosuvastatin approved in ages >=6 years; atorvastatin and simvastatin approved for ages >=10 years). Because the etiology of the disease is the same for both adult and pediatric patients, the overarching goal of therapy is also the same, to lower LDL-C. The current American College of Cardiology/American Heart Association (ACC/AHA) guidelines and the European Atherosclerosis Society (EAS) recommend at least a 50% reduction in LDL-C in all patients with FH to reduce the risk of CVD (Gidding, 2015)(Grundy, 2019)(Wiegman, 2015). The EAS further recommends a target LDL-C <130 mg/dl (3.5 mmol/L) in patients >10 years (Wiegman, 2015). Lipid-lowering therapy should be started as early as possible (Cuchel, 2014) (France, 2016) (Wiegman, 2015).

Angiopoietin-like protein 3 (ANGPTL3) has recently emerged as a target for treatment of elevated levels of LDL-C. Individuals who are homozygous for loss of function (LOF) mutations in ANGPTL3 have lower levels of LDL-C (mean difference of >50% versus control subjects (Minicocci, 2012)). The mechanism by which ANGPTL3 LOF mutations result in lowering LDL-C is not fully understood but appears to be independent of the LDLR. These data suggest that inhibiting ANGPTL3 may be a meaningful and well-tolerated strategy for lowering serum LDL-C in patients with HoFH, especially those considered to have LDLR negative mutations in both alleles.

Evinacumab (REGN1500) is a fully human monoclonal antibody (mAb), created with Regeneron*s VelocImmune® technology platform, which specifically binds to and inhibits ANGPTL3. In an open-label, single-arm, proof-of-concept study in patients with HoFH (R1500 CL-1331), evinacumab demonstrated a mean percent reduction from baseline of 49.2% (n=9) at week 4, 2 weeks after a single dose of 15 mg/kg IV, with a duration of effect of at least 10 weeks (n=7). A peak mean reduction of 52.1% was observed at week 6. Three patients in the study had null/null mutations in the LDLR. Treatment with evinacumab in these difficult-to-treat patients reduced LDL-C by an average of 37.3% at week 4 with peak reductions up to 59.5%.

The LDL-C lowering effect observed with evinacumab in the R1500-CL-1331 study was confirmed in study R1500-CL-1629, a large randomized, double-blind, placebo-controlled study consisting of adult and adolescent patients with HoFH. On average, patients entered the trial with a mean baseline LDL-C of 255 mg/dL, despite treatment with other lipid-lowering therapies, including maximally-tolerated statins, PCSK9 inhibitors, ezetimibe, LDL apheresis and lomitapide. The trial met its primary endpoint, showing that adding evinacumab

to other lipid lowering therapies decreased LDL-C by a mean of 49% from baseline to week 24, compared to lipid-lowering therapies alone (47% reduction for evinacumab compared to a 2% increase for placebo, p<0.0001). This reduction translates to a mean absolute change in LDL-C of 132 mg/dL from baseline, compared to placebo (135 mg/dL reduction for evinacumab compared to a 3 mg/dL reduction for placebo, p<0.0001). The decreases in LDL-C were observed from the first lipid assessment at week 2 and were maintained throughout the 24-week double-blind treatment period. Importantly, similar levels of LDL-C lowering were observed in the most difficult-to-treat null/null or negative/negative patients. The dramatic reduction in LDL C led to the achievement of LDL-C levels <100 mg/dL in 47% of the patients treated with evinacumab compared to 23% treated with placebo (nominal p=0.0203). Evinacumab also reduced apolipoprotein B (Apo B), non-high-density lipoprotein (HDL) cholesterol (non HDL C) and total cholesterol (TC) compared to placebo.
The positive efficacy data in the R1500-CL-1629 study were accompanied by an acceptable safety profile. Evinacumab was generally well-tolerated. During the double-blind treatment period, 66% of evinacumab patients and 81% of placebo patients experienced an adverse event (AE). AEs that occurred in at least 5% of patients and more commonly with evinacumab were influenza-like illness (11% evinacumab, 0% placebo) and rhinorrhea (7% evinacumab, 0% placebo). During the double-blind treatment period there was no difference in the incidence of nausea, abdominal pain or diarrhea between treatment groups, and there were no deaths, major adverse cardiovascular events or findings related to hepatic disorders.
The primary purpose of this current study is to demonstrate the efficacy, safety and tolerability of evinacumab in pediatric patients, aged 5 through 11 years, with HoFH. The study will consist of 3 parts: Part A (phase 1b), Part B (phase 3), and Part C (phase 3). Part A is a single-dose, open label study to determine the safety, pharmacokinetics (PK) and pharmacodynamics (PD) of evinacumab 15 mg/kg intravenous (IV) in approximately 6 patients ages 5 to 11 years with HoFH. Part B is a 24-week, single-arm, open-label study to assess the efficacy and safety of evinacumab in approximately 14 pediatric patients with HoFH. Part B will begin when PK data from all patients in Part A have been sufficiently analyzed to determine the dose for Part B. Part C is an extension of the study available to patients who complete Part A or Part B to continue to receive evinacumab.
Additional background information on the study drug and development program can be found in the Investigator*s Brochure.

**Study objective**

Primary
The primary objective for Part A of the study is to assess the pharmacokinetics (PK) of evinacumab in pediatric patients with homozygous familial hypercholesterolemia (HoFH).
The primary objective for Part B of the study is to demonstrate a reduction of low-density lipoprotein (LDL) cholesterol (LDL-C) by evinacumab in pediatric (5

to 11 years of age) patients with HoFH.

Secondary
The secondary objective for Part A of the study is to evaluate the safety and tolerability of evinacumab administered IV in pediatric patients with HoFH
The secondary objectives for Part B of the study are:
• To evaluate the effect of evinacumab on other lipid parameters (ie, Apo B, non-HDL-C, TC, lipoprotein a [Lp(a)]) in pediatric patients with HoFH
• To evaluate the safety and tolerability of evinacumab administered IV in pediatric patients with HoFH
• To assess the PK of evinacumab in pediatric patients with HoFH
• To assess the immunogenicity of evinacumab in pediatric patients with HoFH over time
• To evaluate patient efficacy by mutation status

**Study design**

Part A is a phase 1B single-dose, open-label study to determine the safety, PK and pharmacodynamics (PD) of evinacumab 15 mg/kg intravenous (IV) in approximately 6 patients ages 5 to 11 years with HoFH. To ensure a distribution of body weight within Part A of the study, every effort will be made to enroll 3 patients <25 kg and 3 patients >=25 kg. Additionally, to ensure a distribution of ages, every effort will be made to enroll 2 patients <10 years of age. All patients who successfully complete Part A may continue receiving evinacumab in an extension of the study, Part C. Initially, patients from Part A who enter the Part C will receive evinacumab 15 mg/kg IV Q4W. When PK data from all patients in Part A have been sufficiently analyzed, the dose for Part B will be determined using the cumulative data to date with evinacumab and data from Part A. If data from 6 patients is insufficient, up to 4 more patients may be enrolled to confirm the dose in Part B. The dose for Part B will also be the final dose in Part C. The dose for Part B (and final dose in Part C) will likely remain at 15 mg/kg IV every 4 weeks (Q4W). However, there is a small possibility that the exposure analysis or the observed PD effect indicate a small increase in the dose is needed for the pediatric population to match the exposure and PD effect observed in adult patients. As such, the dose in Part B (and final dose in Part C) could be between 15-20 mg/kg IV Q4W. A maximum dose of 20 mg/kg is selected as the top dose because it is the highest dose evaluated in the prior evinacumab studies.
Part A consists of up to 4 periods: run-in, screening, single-dose, open-label treatment, and 16-week observation. Upon completion of Part A, patients will have the opportunity to continue into Part C.

Part B is a phase 3 single-arm, open-label study to assess the efficacy and safety of evinacumab in pediatric patients (age 5 to 11 years) with HoFH. Part B will begin once dose-selection for Part B has been completed. Part B will enroll approximately 14 pediatric patients. Patients enrolled in Part B will not include patients from Part A. Upon completion of Part B, patients will have

the opportunity to continue into the extension, Part C.
Part B consists of up to 4 periods: run-in, screening, 24-week open-label treatment, and follow-up (for patients who do not enter the extension, Part C).

Part C is an extension of the study for patients from both Part A and Part B and consists of 2 periods, a 48-week treatment period and a 24-week follow-up period after the last dose of study drug. All patients from Part A who enter Part C will initially receive open-label evinacumab 15 mg/kg IV Q4W. The final dose in Part C will be the same as the dose in Part B; therefore, the dose in Part C could be adjusted to align with the dose in Part B. Patients who are receiving background LMT or who are undergoing apheresis should make every effort to maintain a stable LMT and a stable apheresis schedule (as applicable) throughout the duration of the study to the end of the study. The frequency of apheresis may be reduced during this part of the study based on the investigator*s judgement. The Sponsor of this study, consistent with our corporate policy governing access to investigational drugs in confirmatory clinical studies, is committed to provide evinacumab to patients after their participation in this trial has concluded, if permitted per local laws.
Agreement to continue treatment beyond this study is a treatment decision that must be made by the investigator, and the patient or their parent/guardian. After completion of the study, investigators interested in continuing treatment with evinacumab in patients considered to have a positive response can discuss post-trial treatment options with the Sponsor, including participation in a CUP or EAP.

**Intervention**

For Part A, a single administration of evinacumab 15 mg/kg IV, given over a 65 minute infusion
For Part B, evinacumab with a dose determined by Part A, will be administered IV over a 65 minute infusion Q4W starting at day 1. The last dose will be at week 20.
All patients from Part A who enter Part C will initially receive evinacumab 15 mg/kg IV Q4W. The final dose for Part C will be based on data from Part A and all available data from other evinacumab studies. Therefore, the dose for Part C for patients from Part A may be adjusted once the dose selection for Part B is completed.

**Study burden and risks**

Patients with HoFH have extremely high LDL-C levels are far from their target level and will require significant reductions to get to their treatment goal. Statins are the only pharmacological LMT approved for use in pediatric patients below the age of 10. Unfortunately, they are unable to lower LDL-C sufficiently, even when used in the highest doses and in combination with other therapies. Moreover, the unmet need is greatest in patients with null/null

mutations of the LDLR who typically have the highest levels of LDL-C and in whom statins have minimum to no effects. In addition to pharmacologic treatment, lipoprotein apheresis is the standard of care for pediatric patients with HoFH. However, the availability of lipoprotein apheresis is limited, and the procedure is expensive, invasive and burdensome for young children and their caregivers. Therefore, there is a high unmet need for additional therapeutic options for pediatric patients with HoFH. Evinacumab could be a new addition to the armamentarium of LMT that could contribute to lowering the LDL-C of HoFH pediatric patients, including patients with null/null mutations.
In study R1500-CL-1331, evinacumab demonstrated a mean percent reduction from baseline of 49.2% (n=9) at week 4, 2 weeks after a single dose of 15 mg/kg IV, with a duration of effect of at least 10 weeks (n=7). A peak mean reduction of 52.1% was observed at week 6. Three patients in the study had null/null mutations in the LDLR. Treatment with evinacumab in these difficult to-treat patients reduced LDL-C by an average of 37.3% at week 4 with peak reductions up to 59.5%. The LDL-C lowering effect observed with evinacumab in the R1500-CL-1331 study was confirmed in study R1500-CL-1629, a large randomized, double-blind, placebo-controlled study consisting of adult and adolescent patients with HoFH. On average, patients entered the trial with a mean baseline LDL-C of 255 mg/dL, despite treatment with other lipid lowering therapies, including maximally-tolerated statins, PCSK9 inhibitors, ezetimibe, LDL apheresis and lomitapide. The trial met its primary endpoint, showing that adding evinacumab to other lipid-lowering therapies decreased LDL-C by a mean of 49% from baseline to week 24, compared to lipid-lowering therapies alone (47% reduction for evinacumab compared to a 2% increase for placebo, $p<0.0001$). This reduction translated in this study to a mean absolute change in LDL-C of 132 mg/dL from baseline, compared to placebo (135 mg/dL reduction for evinacumab compared to a 3 mg/dL reduction for placebo, $p<0.0001$). The decreases in LDL-C were observed from the first lipid assessment at week 2 and were maintained throughout the 24-week double-blind treatment period. Importantly, similar levels of LDL-C lowering were observed in the most difficult-to-treat null/null or negative/negative patients. The dramatic reduction in LDL-C led to the achievement of LDL-C levels <100 mg/dL in 47% of the patients treated with evinacumab compared to 23% treated with placebo (nominal $p=0.0203$). Evinacumab also reduced Apo B, non-HDL-C and TC compared to placebo. Based on these data in adults, it is expected that the addition of evinacumab to existing treatments will lead to significant LDL-C reductions in the pediatric HoFH population.
In non-FH populations, numerous epidemiological studies and CV outcomes studies with lipid lowering therapies have continually demonstrated that lowering LDL-C reduces the risk of CV events. In fact, the body of evidence from the statin literature shows that the relationship between LDL-C reduction and CV event reduction is approximately linear and for every 1 mmol/L (38.7 mg/dL) reduction in LDL-C there is a corresponding 22% risk reduction in CV events (Baigent, 2010). Moreover, results from recent outcomes trials with ezetimibe (IMPROVE-IT (Cannon, 2015)), alirocumab (ODYSSEY OUTCOMES (Schwartz, 2018)) and evolocumab (FOURIER (Sabatine, 2017)) reinforce this concept, providing additional

evidence for the relationship between LDL-C lowering through diverse mechanisms and reductions in CV events. Within the context of this study in the HoFH pediatric patient population, additional reductions in LDL-C at an early age may get patients closer to their LDL-C target and maintaining these levels could translate into significant benefit in reducing CV risk.
It is also expected that treatment with evinacumab will be well tolerated and have an acceptable safety profile. The accumulated safety information from the most recent phase 2 and phase 3 studies where evinacumab was given IV in patients with HoFH (R1500 CL 1629, R1500 CL 1719) or persistent hypercholesterolemia (R1500-CL-1643) shows that the more common adverse events across all the studies include Nasopharyngitis, Rhinorrhoea, Upper respiratory tract infection, Influenza-like illness, Back pain, Pain in extremity, Dizziness, Headache, Nausea, Abdominal pain, and Fatigue.
A review of all available safety data shows there is one identified risk of Systemic hypersensitivity reactions, including Infusion reactions, and rarely Anaphylaxis. In most cases, the allergic reactions were mild to moderate in intensity, nonserious and, in the case of infusion reactions, did not lead to interruption or discontinuation of the evinacumab infusion. One event of Anaphylaxis was observed in the phase 2 dose ranging study in patients with severe hypercholesterolemia (R1500-CL-1643). Briefly, the anaphylactic reaction was reported in a single patient randomized to the evinacumab 15 mg/kg IV treatment group. This patient with relevant medical history of syncope, palpitations, asthma, obesity, and seasonal allergy experienced an anaphylactic reaction during the second infusion of evinacumab on study day 28. Within 5 minutes of initiating the infusion, the patient felt dizzy with a racing heart, followed by chest pressure, arms and legs tingling, shortness of breath, itchiness, and feeling warm and lethargic. The patient was noticeably flushed with face and chest redness. The infusion was stopped. The patient was treated with diphenhydramine orally due to continued itching. The event was considered resolved on the same day. The investigator assessed the event as moderate in severity and related to study treatment. Study treatment was permanently discontinued. Further details of this event are provided in the Investigator*s Brochure.
The important potential risks include immunogenicity and embryofetal toxicity. These risks will be managed through careful patient selection and monitoring. Additionally, any potential effects of evinacumab on a child*s development during childhood and early adolescence will be monitored via Tanner staging, sex hormones, and overall growth by tracking weight and height.
A risk-benefit statement with respect to the overall development program is provided in the Investigator*s Brochure.
Recognizing that the *Coronavirus Disease 2019* (COVID-19) pandemic will have an impact on the conduct of clinical trials, the Sponsor does not intend to screen any patients in this study until the impact of the COVID-19 pandemic is deemed manageable and no longer interfering with the conduct of trials at individual sites, and patients can safely participate in this study. Until then, the Sponsor plans to obtain approvals from Health Authorities/Ethics Committees to enable initiation of study sites for this study, as allowed by

local laws and regulations.

## Contacts

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US
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US

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Children (2-11 years)

### Inclusion criteria

1. Males and females ages 5 to 11 years at the time of the screening visit
2. Diagnosis of functional HoFH by either genetic or clinical criteria as defined in the protocol
3. LDL-C >130 mg/dL at the screening visit
4. Body weight >=15 kg
5. Receiving stable maximally tolerated therapy*at the screening visit
*Maximally tolerated therapy could include a daily statin.
6. Willing and able to comply with clinic visits and study-related procedures
7. Parent(s) or legal guardian(s) must provide the signed informed consent form (ICF). Patients >=5 years of age (or above age determined by the IRB/EC and

in accordance with the local regulations and requirements) must also provide informed assent forms (IAFs) to enroll in the study, and sign and date a separate IAF or ICF signed by the parent(s)/legal guardian(s) (as appropriate based on local regulations and requirements)

### Exclusion criteria

1. Background pharmacologic LMT, nutraceuticals or over-the-counter (OTC) therapies known to affect lipids, at a dose/regimen that has not been stable for at least 4 weeks (8 weeks for PCSK9 inhibitors) before the screening visit and patient is unwilling to enter the run-in period
2. For patients entering Part A, unable to temporarily discontinue apheresis from the baseline visit through the week 4 visit
3. Receiving lipid apheresis, a setting (if applicable) and schedule that has not been stable for approximately 8 weeks before the screening visit or an apheresis schedule that is not anticipated to be stable over the duration of the treatment period (48 weeks). A stable schedule is defined as a weekly (every 7±1 days) or every other week (every 14±2 days) schedule
4. Plasmapheresis within 8 weeks of the screening visit, or plans to undergo plasmapheresis during Part A or Part B.
5. Presence of any clinically significant uncontrolled endocrine disease known to influence serum lipids or lipoproteins
6. Newly diagnosed (within 3 months prior to randomization visit [week 0/day 1]) diabetes mellitus or poorly controlled (hemoglobin A1c [HbA1c] >9%) diabetes

Additional exclusion criteria apply, please refer to the protocol

## Study design

### Design

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|---|---|
| Study phase: | 3 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 25-11-2020 |
| Enrollment: | 3 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | evinacumab |
| Generic name: | evinacumab |

# Ethics review

| | |
|---|---|
| Approved WMO Date: | 30-07-2020 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 03-11-2020 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 15-08-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 13-10-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 18-07-2022 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO | |

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|---|---|
| Date: | 21-10-2022 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2019-001931-30-NL |
| ClinicalTrials.gov | NCT04233918 |
| CCMO | NL72762.018.20 |