# A 2-Part, Phase 2/3 Study to Assess the Safety, Tolerability and Efficacy of AMG 145 in Subjects With Homozygous Familial Hypercholesterolemia
# Part A - Open-label, Single-arm, Multicenter Pilot Study to Evaluate Safety,
# Tolerability, and Efficacy of AMG 145 in Subjects With Homozygous Familial Hypercholesterolemia
# Part B - Double-blind, Randomized, Placebo-controlled, Multicenter Study to Evaluate Safety, Tolerability and Efficacy of AMG 145 in Subjects

Published: 03-07-2013
Last updated: 23-04-2024

Primary ObjectivePart A: To characterize the effect of 12 weeks of subcutaneous (SC) AMG 145 on percentchange from baseline in low-density lipoprotein cholesterol (LDL-C) in subjects with homozygousfamilial hypercholesterolemiaPart B: To evaluate...

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Metabolic and nutritional disorders congenital |
| **Study type** | Interventional |

## Summary

## ID

NL-OMON38555

**Source**
ToetsingOnline

**Brief title**
TESLA - 20110233

## Condition

- Metabolic and nutritional disorders congenital

**Synonym**
hypercholesterolemia; elevated cholesterol

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Amgen
**Source(s) of monetary or material Support:** Amgen BV

## Intervention

**Keyword:** AMG 145, Homozygous Familial Hypercholesterolemia

## Outcome measures

### Primary outcome

percentage change from baseline LDL-C at week 12. 8 visits; 8 visits fasting.

Duration 2h.

### Secondary outcome

Adverse events, absolute change LDL-C baseline to week 12, % change baseline to

week 12 of: non-HDL-C, ApoB en LP(a)

# Study description

## Background summary

Homozygous Familial Hypercholesterolemia is a rare disease. The homozygous form occurs in 1: 1,000,000 patients. The severity of cardiovascular disorders in homozygote patients is higher than with the familial hypercholesterolemia patients
Many patients with homozygous hypercholesterolemia fail to reach goal even with maximal use of stantis and other add on agents such as ezetimibe or niacin. There is a major unmet medical need for a much more effective add-on than ezetimibe in these patients. AMG 145 is a fully human monoclonal immunoglobulin (Ig) G2 that binds specifically to human proprotein convertase subtilisin/kexin type 9 (PCSK9) and prevents the interaction of PCSK9 with the LDL receptor. AMG 145 caused a dose related inhibition of PCSK9 binding to the LDL receptor and of tthe PCSK9-mediated reduction in low-density lipoprotein (LDL) uptake in hepatic cells. Treatment of cells with a combination of AMG 145 and statin increased LDL receptor protein levels more than treatment with with either alone. Single administartions in humans produces decreases in mean LDL-C with subsequent returns to baseline. Across the dose groups, the decreases were dose-related. Overall, AMG 145 appeared to be well tolerated at the IV and SC doses administered in the FIH study. Incidences of overall adverse events and treatment-related adverse event did not difer notable between treatmentgroups. The present study is designed to evaluate the effects of a subcutaneous AMG 145 every 4 weeks compared to placebo, in terms of efficacy and safety in subjects with homozygous hypercholesterolemia.

## Study objective

Primary Objective
Part A: To characterize the effect of 12 weeks of subcutaneous (SC) AMG 145 on percent
change from baseline in low-density lipoprotein cholesterol (LDL-C) in subjects with homozygous
familial hypercholesterolemia
Part B: To evaluate the effect of 12 weeks of subcutaneous (SC) AMG 145 compared with
placebo on percent change from baseline in LDL-C in subjects with homozygous familial
hypercholesterolemia

## Study design

If Part A of this study is successful, approximately 51 new subjects will be enrolled into Part B.
Subjects enrolled into this Phase 3 study will be randomized to a 2:1 allocation into two treatment
groups: 420 mg AMG 145 Q4W SC or placebo Q4W SC. Randomization will be

stratified by
baseline LDL-C levels. Study visits will occur every 2 weeks.

**Intervention**

Treatment with AMG 145 or placebo every 4 weeks

**Study burden and risks**

Risk: Adverse effects of study medication
Burden: Max. study duration approx. 20 weeks. 3 sc injections per visit, 3x1 ml every time
Physical examination 3 x.
Bood test 6-8 x 20 - 30 ml per occassion
Sample for biomarker development 60 ml
Urine tests 2x
ECG 2x
Dietary instructions

# Contacts

**Public**
Amgen

Minervum 7061
Breda 4800 DH
NL
**Scientific**
Amgen

Minervum 7061
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NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

Males and females, * 12 to * 80 years of age with a diagnosis of homozygous familial hypercholesterolemia by genetic confirmation or a clinical diagnosis based on a history of an untreated LDL cholesterol concentration greater than 500 mg/dL (13 mmol/L) together with either
xanthoma before 10 years of age or evidence of heterozygous familial hypercholesterolemia in
both parents.
For enrollment, subjects have to be stable on a low-fat diet and their pre-existing, lipid-lowering
therapies (such as statins, cholesterol-absorption inhibitors, bile-acid sequestrants, nicotinic acid,
or combinations thereof) for at least 4 weeks, with fasting central lab LDL cholesterol concentration >130 mg/dL (3.4 mmol/L), central lab triglyceride concentration < 400 mg/dL (4.5 mmol/L), and bodyweight of 40 kg or greater at screening. Patients are should not change
their background lipid-lowering drug during the trial.

## Exclusion criteria

LDL or plasma apheresis within 8 weeks prior to enrollment; use of
Mipomersen within 5 months of screening; New York Heart Failure Association (NYHA) class III or IV or last known left ventricular ejection fraction < 30%; cardiac arrhythmia within past 3 months that is not controlled by medication; myocardial infarction, unstable angina, percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG) or stroke within
3 months of enrollment; planned cardiac surgery or revascularization; systolic blood pressure (SBP) > 180 mmHg or diastolic BP (DBP) > 110 mmHg; requiring statin up-titration within 4 weeks of screening; estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73m2; persistent
aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 3x ULN, creatine kinase
(CK) > 5x ULN without a known source; known major active infection, or major hematologic, renal, metabolic, gastrointestinal or endocrine dysfunction; deep vein thrombosis or pulmonary
embolism within 3 months prior to enrollment.

# 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): | 04-11-2013 |
| Enrollment: | 3 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | AMG 145 |
| Generic name: | AMG 145 |

# Ethics review

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|---|---|
| Approved WMO Date: | 03-07-2013 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 23-08-2013 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO | |

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|---|---|
| Date: | 24-09-2013 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 03-02-2014 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 11-02-2014 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 09-10-2014 |
| 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 |
|---|---|
| Other | clinicaltrials.gov |
| EudraCT | EUCTR2011-005399-40-NL |
| CCMO | NL44583.018.13 |