

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

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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...

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 statins 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 the 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 either alone. Single administrations 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 differ notably between treatment groups. 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

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NL

Scientific

Amgen

Minervum 7061

Breda 4800 DH

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

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	

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