A Multicenter, Open-label Study to Assess the Long-term Safety, Tolerability, and Efficacy of AMG 145 on LDL-C in Subjects With Severe Familial Hypercholesterolemia

Published: 04-07-2013
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Primary Objective: To characterize the safety and tolerability of long-term administration ofAMG 145 among subjects with severe familial hypercholesterolemia

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

Summary

ID

NL-OMON40135

Source
ToetsingOnline

Brief title
TAUSSIG - 20110271

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, Familial Hypercholesterolemia

Outcome measures

Primary outcome

Subject incidence of treatment emergent adverse events

Secondary outcome

Percent change in LDL-C from baseline at each scheduled visit

• Percent change in non-HDL-C from baseline at each scheduled visit

• Percent change in ApoB from baseline at each scheduled vist

• Percent change in Lp(a) from baseline at each scheduled visit

• Percent change in total cholesterol/HDL-C ratio from baseline at each

scheduled visit

• Percent change in ApoB/ApoA1 ratio from baseline at each scheduled visit

Study description

Background summary

Homozygous or severe 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 or severe 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: To characterize the safety and tolerability of long-term administration of
AMG 145 among subjects with severe familial hypercholesterolemia

Study design

A multicenter, open-label study designed to assess the long-term safety, tolerability, and efficacy of AMG 145. The study will continue for 5 years or until AMG 145
becomes commercially available, whichever is earlier.

Intervention

AMG 145 every four weeks or every 2 weeks for patients with apheresis or patient with pending observed LDL-C levels and
insufficient suppression of PCSK9 (> 100 ng/mL).

Study burden and risks

Risk: Adverse effects of study medication
Burden: Max. study duration 5 years. max 11 visits until week 20. sc injections off 6 ml every four weeks.
Bood test 11 x 20 - 30 ml per occassion
Sample for biomarker development 60 ml
Pregnancy test if relevant every 6 months.
Urine tests 3x
ECG 2x
Dietary instructions

Contacts

Public
Amgen

Minervum 7061
Breda 4800 DH
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 diagnosed with severe familial hypercholesterolemia must meet the following criteria in order to participate in this study:
OR: Completed study 20110233 or a qualifying AMG 145 parent protocol, did not experience a treatment related serious adverse event that led to IP discontinuation, and are still taking investigational product at the end of that study.
OR: Subjects that have not participated in a qualifying AMG 145 parent protocol must also meet all of the following inclusion criteria:
- Are on a stable low-fat diet and taking pre-existing lipid-lowering therapies
- Fasting triglycerides <= 400 mg/dL (4.5 mmol/L)

Exclusion criteria

use of Mipomersen or Lomitapide 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 cause; known major active infection, use of CETP inhibitor in the last 12 months prior to LDL-C screening

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-01-2014
Enrollment:	23
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	04-07-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-09-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-09-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-11-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2015

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-12-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-12-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-08-2016

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-08-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-09-2017
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	EUCTR2012-003165-32-NL
CCMO	NL44594.018.13