A Multicenter, Controlled, Open-label Extension (OLE) Study to Assess the Long-term Safety and Efficacy of AMG 145

Published: 17-06-2013
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Primary: To collect long-term safety data.Secondary objectives: To collect long-term efficacy data (LDL-C).

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lipid metabolism disorders
Study type	Interventional

Summary

ID

NL-OMON45229

Source
ToetsingOnline

Brief title
OSLER 2

Condition

- Lipid metabolism disorders

Synonym
dyslipidemia; elevated cholesterol

Research involving
Human

Sponsors and support

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

Intervention

Keyword: AMG 145, dyslipidemia, long-term, OSLER2

Outcome measures

Primary outcome

Adverse events.

Secondary outcome

LDL-C at week 48 and 104.

Study description

Background summary

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 produced 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 this FIH study. Incidences of overall adverse events and treatment-related adverse events did not differ notably between treatment groups.
De current study is an extension of 3 studies with AMG 145 that are currently being executed in the Netherlands:

1. A Double-blind, Randomized, Placebo and Ezetimibe Controlled, Multicenter Study to Evaluate Safety, Tolerability and Efficacy of AMG 145 on LDL-C in Combination With Statin Therapy in Subjects With Primary Hypercholesterolemia and Mixed Dyslipidemia (AMG 145 20110115)
EudraCT number: 2012-001363-70, CCMO number NL40964.018.12.

2. A Double-blind, Randomized, Multicenter Study to Evaluate Safety and Efficacy of AMG 145, Compared With Ezetimibe, in Hypercholesterolemic Subjects Unable to Tolerate an Effective Dose of a HMG-CoA Reductase Inhibitor (AMG 145 20110116)

EudraCT number: 2012-001364-30, CCMO number NL40965.018.12

3. A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Evaluate Safety, Tolerability and Efficacy of AMG 145 on LDL-C in Subjects with Heterozygous Familial Hypercholesterolemia (AMG 145 20110117)
EudraCT number: 2012-001365-32, CCMO number NL40966.018.12

4. A Double-blind, Randomized, Multicenter Study to Evaluate the Safety and Efficacy of AMG 145, Compared With Ezetimibe, in Hypercholesterolemic Subjects Unable to Tolerate an Effective Dose of a HMG-CoA Reductase Inhibitor Due to Muscle Related Side Effects
EudraCT nummer: 2013-000935-29, CCMO nummer NL46854.018.14 (AMG145 20120332 GAUSS-3, this study only takes place at sites AMC and SFG)

Subjects who have completed one of the parent studies and do not discontinue IP in the parent study for any reason including an adverse event will be eligible for this extension study. The GAUSS-3 study is a study for statin intolerant patients and consists of 3 parts. In part A subjects will be actively rechallenged on statin therapy. Only subjust that have a proven statin intolerance in aprt A will continue into part B (AMG145 vs ezetimibe) and part C (open label AMG 145). it is expected that 20% of the subjects in part A will continue into part B/C. Subject that cannot continue into part B of the study can roll-over into teh OSLER-2 study.

The main objective of the extension study is to collect long-term safety data.

Study objective

Primary: To collect long-term safety data.
Secondary objectives: To collect long-term efficacy data (LDL-C).

Study design

Multicenter randomized open-label phase III extension study.
Randomization (2:1) within 30 days after the end of the parent study to:
* AMG 145 plus standard of care
* Standard of care.
Patient may choose between injections AMG 145 every 2 weeks (140 mg s.c.) or every month (420 mg s.c.). AMG 145 injections will be administered by the patient via the auto innjector pen or 3.5 ml personal injector (if available)
During the first 12 weeks LDL-C will remain blinded (investigator will be informed if triglycerides are > 11.3 mmol/L) and subjects must remain on stable background lipid lowering therapy. Background lipid lowering therapy: therapy either prescribed to the subject prior to participation in parent study or statin or ezetimibe therapy given during parent study.
After week 48 all subjects will receive open-label AMG 145 for approximately 2

year.
Approx. 4500 patients.

Intervention

Treatment with AMG 145.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: Study duration approx. 2 years. Visits every 12 weeks.
Every month collection of injection(s) to be self-adminsitered and discussion of any signs or symptoms.
Two additional visits for training of self-injection for those patients not yet familiar with self-injection.
Additional full visit in week 60 for those who have received AMG 145 after the first 48 weeks for the first time ever.
AMG 145 s.c.: 1 injection (1 mL) every 2 weeks or 3 injections (1 mL) every month during 104 or 56 weeks via the auto injector of 3.5 ml personal injector (if available)
Physical examination 2x.
Blood tests 7x (fasting), 30-60 ml/occasion.
Urine tests 6x.

Contacts

Public
Amgen

Minervum 7061
Breda 4817 ZK
NL
Scientific
Amgen

Minervum 7061
Breda 4817 ZK
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Subjects will be eligible for the study if they complete a qualifying AMG 145 parent study protocol while still on assigned study medication.

Exclusion criteria

Subjects will be ineligible for the study if they fulfill any of the following criteria:
1. Discontinued assigned study drug during the qualifying study for any reason including an adverse event or serious adverse event.
2. Female subject is not willing to use an acceptable method(s) of effective birth control during treatment with investigational product (IP) and for an additional 15 weeks after the end of treatment with IP. Female subjects, who have had a hysterectomy, bilateral salpingectomy, bilateral oophorectomy, or who are postmenopausal, are not required to use contraception
o Menopause is defined as 12 months of spontaneous and continuous amenorrhea in a female * 55 years old; or age < 55 years but no spontaneous menses for at least 2 years; or age < 55 years and spontaneous menses within the past 1 year, but currently amenorrheic (eg, spontaneous or secondary to hysterectomy), and with postmenopausal gonadotropin levels (luteinizing hormone and follicle stimulating hormone levels > 40 IU/L) or postmenopausal estradiol levels (<5 ng/dL) or according to the definition of "postmenopausal range" for the laboratory involved.
o Acceptable methods of effective contraception are defined in the ICF. Where required by local laws, regulations and/or guidelines, additional country-specific requirements are outlined in a country-specific protocol supplement.
3. Female subject is pregnant or breast feeding, planning to become pregnant or planning to breastfeed during treatment with IP and/or within 15 weeks after the end of treatment with IP.
4. Unreliability as a study participant based on the investigator's (or designee*s) knowledge of the subject (eg, inability or unwillingness to adhere to the protocol).

5. Disorder that would interfere with understanding and giving informed consent or compliance with protocol requirements.
6. Have an unstable medical condition, in the judgment of the investigator.
7. Subject*s medical condition requires lipid measurement and/or adjustment of background lipid-regulating therapy during the first 12 weeks of study participation.
8. Known sensitivity to any of the products to be administered during dosing.
9. Currently enrolled in another investigational device or drug study (excluding AMG 145 parent study), or less than 30 days since ending another investigational device or drug study(s),or receiving other investigational agent(s).

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-08-2013
Enrollment:	146
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	evolocumab (AMG 145)
Generic name:	evolocumab (AMG 145)

Ethics review

Approved WMO Date:	17-06-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-06-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-06-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-07-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-08-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-03-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	26-03-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-05-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-06-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-07-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-12-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	30-01-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-05-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-07-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-08-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-09-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-09-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-12-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-01-2016

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-04-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-05-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-06-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-07-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-07-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-07-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-08-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	06-09-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-09-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-11-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-11-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-09-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-10-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-11-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	clinical trials.gov; registratienummer n.n.b.
EudraCT	EUCTR2012-004357-83-NL
CCMO	NL44053.060.13