AN OPEN-LABEL, SINGLE-ARM, PROOF-OF-CONCEPT STUDY TO EVALUATE THE SAFETY AND EFFICACY OF SINGLE AND MULTIPLE DOSES OF REGN1500 IN PATIENTS WITH HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA

Published: 17-05-2016
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Please refer to protocol, section 1.2 "Rationale"

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON43236

Source
ToetsingOnline

Brief title
Safety/efficacy study in patients with Hereditary high cholesterol

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- 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: Regeneron Pharmaceuticals;Inc.

Intervention

Keyword: efficacy, high cholesterol, Phase 2, safety

Outcome measures

Primary outcome

The primary endpoint in the study is the percent change in LDL-C from baseline (week 0) to week 4.

Secondary outcome

The secondary endpoints are:

- The percent and absolute change in LDL-C from week 2 to week 4

- The percent and absolute change from baseline in LDL-C over time in the main study period

- The percent and absolute change in LDL-C from baseline to every scheduled post-baseline visit up to week 38, and weeks 42, 46, 50, 54, 58, and every 24 weeks afterwards in the OLE period

- The absolute change in LDL-C from baseline (week 0) to week 4

- The percent and absolute change from baseline in Apo B, non-HDL-C, total-C, and Lp (a) over time in the main study period

- The percent and absolute change in Apo B, non-HDL-C, total-C, and Lp (a) from baseline to every scheduled post-baseline visit based on the schedule of the specialty lipid panel in the OLE period

- The proportion of patients who achieve a reduction in LDL-C of *15% from

baseline in both the main study period and the OLE

- The proportion of patients with *30% reduction in LDL-C from baseline in both the main study period and the OLE period

- The percent and absolute change in HDL-C, triglycerides, and Apo A-1 over time in the main study period

- The percent and absolute change in HDL-C, triglycerides, and Apo A-1 from baseline to every scheduled post-baseline visit based on the schedule of the specialty lipid panel in the OLE period

- The percent and absolute change from baseline in Apo CIII over time in the main study period

- The percent and absolute change in Apo CIII from baseline to every scheduled post-baseline visit based on the schedule of the specialty lipid panel in the OLE period

- The incidence and severity of treatment-emergent adverse events (TEAEs) reported from the first dose of study drug to the end of study or the last visit in patients treated with REGN1500

- Serum concentration of REGN1500 over time and other PK parameters

- Presence and titer of anti-REGN1500 antibodies over time

Study description

Background summary

Please refer to protocol, section 1.1 "Introduction"

Study objective

Please refer to protocol, section 1.2 "Rationale"

Study design

This is an open-label, single-arm study in patients with HoFH. The study consists of 6 periods: a run-in (for patients whose background LMT has not been stable prior to screening or who have undergone lipid-apheresis within 4 weeks of screening), screening, a main study open-label treatment period, an observation period and an open-label extension (OLE) treatment period, and an OLE follow-up period.

Run-In:
Patients whose background medical LMT has not been stable for at least 4 weeks (6 weeks for fibrates) prior to the screening visit (week -2) or who have undergone lipid-apheresis within 4 weeks prior to the screening visit (week -2) will enter a run-in period (4 weeks to stabilize LMT other than fibrates; 6 weeks to stabilize fibrate therapy, and 4 weeks to wash out of lipidapheresis therapy).

Screening:
Patients who have been on a stable background medical LMT for at least 4 weeks (6 weeks for fibrates) prior to the screening visit (week -2) or who have not undergone lipid apheresis within 4 weeks prior to the screening visit (week -2) will directly enter a 2-week screening period. Background (stable) lomitapide is permitted, with sponsor approval prior to enrollment, in up to 4 patients. Rescreening of patients may be permitted on a case-by-case basis, following a full review and approval by the study medical monitor. Patients who are determined to be eligible for rescreening must be reconsented and undergo all screening evaluations.

Main Study Open-Label Treatment:
Patients who meet all inclusion criteria and none of the exclusion criteria will be enrolled to receive a singel open-label dose of REGN1500 at 15 mg/kg IV at week 2 (day 15).

Observation Period:
Patients will be followed for a period of 24 weeks (through week 26 [day 183]) after the last dose of study drug in the main study period.

Open-Label Extension Treatment Period:
Patients who meet the eligibility criteria for the OLE will be enrolled to continue treatment. The OLE period will last approximately 4 years, from week 26 (day 183) through week 214 (day 1493). It is estimated that this period will last either until REGN1500 is available commercially, or until the program is terminated, whichever comes first. Patients who still meet eligibility criteria will receive 4 weekly 300 mg subcutaneous (SC) doses of REGN1500 starting at week 26 (day 183). They will then receive a 20 mg/kg

intravenous (IV) dose of REGN1500 at week 38 (day 267). Starting at week 58 (day 407), patients will receive a 20 mg/kg IV dose of REGN1500 every 12 weeks, through week 178 (day 1247).

Open-Label Extension Follow-up Period:
Patients will be followed for a period of 24 weeks (through week 214 [day 149]) after the last dose of study drug in the OLE treatment period.

Study Duration:
The maximum duration of the main study per patient is up to approximately 34 weeks (approximately 8.5 months): up to 8 weeks for run-in/screening, 2 weeks for the open-label treatment period, and 24 weeks of follow-up in the observation period. The planned duration of the OLE is up to an additional 4 years.

Intervention

In the main portion of the study, eligible patients will be enrolled to receive a single open-label dose of REGN1500 at 15 mg/kg IV at week 2 (day 15).
In the OLE potion of the study, patients will receive open label REGN1500 in all of the following schedules:
* REGN1500 at 300 mg SC once weekly for 4 weeks starting at week 26 (day 183)
* REGN1500 at 20 mg/kg IV at week 38 (day 267)
* REGN1500 at 20 mg/kg IV every 12 weeks from week 58 (day 407) through week 178 (day 1247)

Study burden and risks

Please refer to IMPD, page 869 "Risk Benefit Assessment"

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Men and women *18 years of age at the time of the screening visit;
2. Diagnosis of Homozygous Familial Hypercholesterolemia (HoFH);
3. Willing to consistently maintain usual diet for the duration of the study;
Please refer to the Protocl for a full list of Inclusion criteria.

Exclusion criteria

1. Background medical lipid modifying therapy that has not been stable for at leat 4 weeks (6 weeks for fibrates) prior to the screening visit
2. Having undergone lipid apheresis within 4 weeks prior to the screening visit;
3. Use of another investigational drug or therapy within 30 days or at least 5 half-lives (whichever is longer) prior to the screening visit.
4.Previous participation in any clinical trial of REGN1500
Please refer to the Protocl for a full list of Exclusion criteria.

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):	17-10-2016
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	evinacumab

Ethics review

Approved WMO Date:	17-05-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	15-07-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	23-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	22-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	17-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-01-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-03-2018
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	EUCTR2016-000411-32-NL
ClinicalTrials.gov	NCT02265952
CCMO	NL57302.018.16