An Open-Label Study of Volanesorsen Administered Subcutaneously to Patients with Familial Chylomicronemia Syndrome (FCS)

Published: 10-03-2016
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To evaluate the safety and efficacy of extended dosing with volanesorsen (volanesorsen sodium 300 mg) in patients with FCS

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

Summary

ID

NL-OMON46961

Source
ToetsingOnline

Brief title
ISIS-CS7 study/ APPROACH Open Label

Condition

- Lipid metabolism disorders

Synonym
Familial Chylomicronemia Syndrome (FCS)

Research involving
Human

Sponsors and support

Primary sponsor: Akcea Therapeutics
Source(s) of monetary or material Support: Akcea Therapeutics

Intervention

Keyword: apoC-III, Hypertriglyceridemia, volanesorsen

Outcome measures

Primary outcome

Safety Endpoints:

• Adverse events including adjudicated events of acute pancreatitis and MACE

• Vital signs and weight

• Physical examinations

• Clinical laboratory tests (serum chemistry, hematology, coagulation, urinalysis)

• Echocardiography

• Electrocardiograms (ECGs)

• Use of concomitant medications

• MRIs

Efficacy Endpoints:

• Percent change and absolute change from baseline in fasting TG

• Frequency and severity of patient reported abdominal pain during the treatment period

• Percent change and change from baseline in other fasting lipid measurements including total cholesterol, non-high-density lipoprotein cholesterol (non-HDL-C), apolipoprotein B [apoB], high-density lipoprotein-cholesterol (HDL-C), apolipoprotein A-1 [apoA-1], very-low-density lipoprotein-cholesterol (VLDL-C), and LDL-C

• Percent change from baseline in fasting total apolipoprotein C-III (apoC-III)

• Quality of Life questionnaires (EQ-5D, SF-36)

• Adjudicated acute pancreatitis event rate

• Other symptoms: eruptive xanthoma, lipemia retinalis

Secondary outcome

N/A

Study description

Background summary

Volanesorsen (ISIS 304801) is a second-generation antisense oligonucleotide (ASO) drug targeted to human apoC-III. The hybridization (binding) of ISIS 304801 to the cognate mRNA results in the RNase H-mediated degradation of the apoC-III mRNA, thus preventing production of the apoC-III protein.

Study objective

To evaluate the safety and efficacy of extended dosing with volanesorsen (volanesorsen sodium 300 mg) in patients with FCS

Study design

This is a multi-center, open-label study. Patients who participated earlier with the ISIS 304801-CS6 and ISIS 304801-CS16 studies can participate with this study. All patients will receive volanesorsen 300 mg once per week for 52 weeks. Dietary counseling will be reinforced at intervals throughout the treatment and follow-up period. Following the Week 52 visit, patients can decide if they want to continue with the extended treatment period of 52 weeks . If not, they will enter a 13 week post-treatment evaluation period.

Intervention

All patients will receive volanesorsen 300 mg once per week for 52 weeks.

Study burden and risks

Risks: possible side effects of the medication and study procedures
Burden::Weekly visits to the investigator; at each visit a blood sample is taken. There are a number of mandatory visits, the other visits can be

conducted by a nurse at patient's home. A urine sample is taken at 13 visits (+10 visits if they decide to participate in the extended treatment). Patients are required to fast from all food and drink (except water) for at least 10 hours before each visit. During the whole study, alcohol intake must be limited and patients will need to refrain from drinking any alcohol for at least 48 hours prior to each study visit. Patients need to follow a low-fat diet.

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. Must give written informed consent to participate in the study (signed and dated) and any authorizations required by law
2. Age >= 18 years at time of informed consent
3. Group 1 and 2: Satisfactory completion of ISIS 304801-CS6 or ISIS 304801-CS16 (index

studies) with an acceptable safety profile, per Sponsor and Investigator judgement. ;Group 2: Patients who enrolled in ISIS 304801-CS16 must also meet the following criteria in order to enter into the open-label Study:
a. History of chylomicronemia as evidenced by documentation of lactescent serum (a creamy top layer after ultracentrifugation of a fasting blood sample) or documentation of fasting TG measurement >= 880 mg/dL (10 mmol/L)
b. A diagnosis of Familial Chylomicronemia Syndrome (Type 1 Hyperlipoproteinemia) by documentation of at least one (1) of the following:
• Confirmed homozygote, compound heterozygote or double heterozygote for known loss-of-function mutations in Type 1-causing genes (such as LPL, apoC-II, GPIHBP1, or LMF1)
• Post heparin plasma LPL activity of <= 20% of normal in medical history. Note: testing of LPL activity should not be performed to confirm eligibility for the study
c. Group 2: Fasting TG >= 750 mg/dL (8.4 mmol/L) at Qualification for the ISIS 304801-CS16 study
4. Able and willing to participate in a 65-week study
5. Satisfy one (1) of the following:
a. Females: Non-pregnant and non-lactating; surgically sterile (e.g., tubal occlusion, hysterectomy, bilateral salpingectomy, bilateral oophorectomy), post-menopausal (defined as 12 months of spontaneous amenorrhea in females > 55 years of age or, in females <= 55 years, 12 months of spontaneous amenorrhea without an alternative medical cause and FSH levels in the postmenopausal range for the laboratory involved), abstinent*, or if engaged in sexual relations of child-bearing potential, patient is using an acceptable contraceptive method (refer to Section 6.3.1) from time of signing the informed consent form until 13 weeks after the last dose of Study Drug administration.
b. Males: Surgically sterile, abstinent* or if engaged in sexual relations with a female of child-bearing potential, patient is utilizing an acceptable contraceptive method (refer to Section 6.3.1) from the time of signing the informed consent form until 13 weeks after the last dose of Study Drug administration.
* Abstinence is only acceptable as true abstinence, i.e., when this is in line with the preferred and usual lifestyle of the patient. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods), declaration of abstinence for the duration of a trial and withdrawal are not acceptable methods of contraception.

Exclusion criteria

• Have any new condition or worsening of existing condition which in the opinion of the Investigator would make the patient unsuitable for enrollment, or could interfere with the patient participating in or completing the study
Unwilling to comply with lifestyle requirements for the duration of the study (protocol section 6.3)

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	03-10-2016
Enrollment:	5
Type:	Actual

Ethics review

Approved WMO Date:	10-03-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-07-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-09-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Not approved Date:	21-11-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	12-07-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-07-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-09-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	31-10-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-12-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-01-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-02-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-05-2018
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-06-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2015-003755-21-NL
CCMO	NL56889.000.16

Study results

Date completed:	08-08-2018
Results posted:	27-01-2021
Actual enrolment:	3

First publication
04-12-2020