An Open-Label Extension Study of AKCEA-APOCIII-LRX Administered Subcutaneously to Patients with Familial Chylomicronemia Syndrome (FCS)

Published: 29-04-2022
Last updated: 14-09-2024

This study has been transitioned to CTIS with ID 2023-509029-29-00 check the CTIS register for the current data. In this study, we look at how safe the new medicinal product ISIS 678354 is for the treatment of FCS. And how well it works.

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

Summary

ID

NL-OMON51487

Source
ToetsingOnline

Brief title
ISIS 678354-CS13
OLE

Condition

- Metabolic and nutritional disorders congenital
- Lipid metabolism disorders

Synonym
Familial Chylomicronemia Syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Ionis Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Ionis Pharmaceuticals;inc.

Intervention

Keyword: AKCEA-APOCIII-LRX, Extension study, Familial Chylomicronemia Syndrome

Outcome measures

Primary outcome

Safety endpoints include a proportion of patients who show the following

changes from Baseline to Week 53, week 105 and week 157:*

• Decrease in platelet count by >= 30%

• Decrease in platelet count by >= 50%

• Platelet count value < 50,000 mm3

• Major bleeding events

• Clinically relevant non-major bleeding events

• Decrease in estimated glomerular filtration rate (eGFR) by >= 30%

• Decrease in eGFR by >= 50%

• Urine protein-Creatine ratio (UPCR) >= 1000 mg/g

• Urine albumin-creatine ratio (UACR) >= 500 mg/g

• alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >= 5 ×

upper limit of normal (ULN)

• Total bilirubin >= 2.0 mg/dL

• ALT or AST >= 3 × ULN and total bilirubin >= 2 × ULN

* Lab values based on confirmed results

In addition, rate of major adverse cardiovascular event (MACE) will be

summarized.

Secondary outcome

The efficacy endpoints are the following:

• Percent change in fasting triglcycerides (TG) from Baseline at month 6

(average of Weeks 23, 25 and 27)

• Percent change in fasting TG from Baseline at month 12 (average of Week 51

and 53), month 24 (average of week 103 and 105) , and month 26 (average of week

155 and 157)

• Proportion of patients who achieve >= 40% reduction in fasting TG from

Baseline at month 6

• Proportion of patients who achieve >= 40% reduction in fasting TG from

Baseline at month 12, 24, 36

• Percent change in fasting apoC-III from Baseline at Month 6

• Percent change in fasting apoC-III from Month 12, 24, 36

• Percent change in fasting apoprotein B48 (apoB48) from Baseline at month 6

• Percent change in fasting apoB48 from Baseline at month 12, 24, 36

• Percent change in fasting non-HDL-C from Baseline at Month 6

• Percent change in fasting non-HDL-C from Months 12, 24, 36

• Proportion of patients who achieve fasting TG <= 880 mg/dL at month 6

• Proportion of patients who achieve fasting TG <= 880 mg/dL at month 12, 24, 36

• Adjudicated acute pancreatitis event rate during the Treatment Period (Week 1

through Week 53, 105 or 157), in patients with >= 2 events of adjudicated acute

pancreatitis in 5 years prior to treatment with Study Drug in the index study

• Adjudicated acute pancreatitis event rate during the Treatment Period (Week 1

through Week 53, 105 or 157)

• Adjudicated acute pancreatitis event rate during the Treatment Period

(Week 1 through Weeks 53, 105, or 157) in patients with a prior history of

pancreatitis within 10 years prior to Screening in the index study

• Proportion of patients who achieve >= 70% reduction in fasting TG from

Baseline at month 6

• Proportion of patients who achieve >= 70% reduction in fasting TG from

Baseline at month 12, 24, 36

• Proportion of patients who achieve fasting TG <= 500 mg/dL at month 6

• Proportion of patients who achieve fasting TG <= 500 mg/dL at month 12, 24, 36

Exploratory endpoint:

Health care utilization: Emergency room (ER) visits, hospitalizations, and

total in-patient days

Patient perceived meaningful change in FCS-SIS

Pharmacokinetics endpoint

Pharmacokinetic exposure over time and potential exposure-response analysis

using relevant exposure parameters and biomarkers

Study description

Background summary

Familial Chylomicronemia Syndrome (FCS) is a disease passed on through families. People with FCS have high amounts of fats in their blood. People

with FCS may get fat deposits on their skin. They often experience frequent and severe abdominal pain (stomach area), repetitive cramps and are at a higher risk of developing inflammation of the pancreas. The pancreas is an organ required for a good digestion and blood sugar level. Inflammation of the pancreas can cause severe pain in the stomach area and often requires long stays in the hospital.

Apoliprotein C-III (ApoC-III) is found in blood and increases the fat levels in the blood. The study drug, ISIS 678354, reduces the amount of apoC-III in the blood. This may help people lower the fat in the blood. The study drug could be a treatment for FCS. Health authorities have not approved the study drug for the treatment of FCS. The study drug has previously been tested in healthy volunteers and patients with heart disease and elevated fat levels.

Study objective

This study has been transitioned to CTIS with ID 2023-509029-29-00 check the CTIS register for the current data.

In this study, we look at how safe the new medicinal product ISIS 678354 is for the treatment of FCS. And how well it works.

Study design

This study is an open label extension study of the Balance study (ISIS 678354-CS3). This study will provide the participant with extended treatment of Familial Chylomicronemia Syndrome (FCS) with the study drug. An *open-label* study means that both the participant and the investigator are aware that the participant will be treated with the study drug, ISIS 678354.

During this study, there will be 50 visits during 174 weeks. There are 3 periods to this study:
1. Screening (2 visits): up to 31 days (4 weeks)
Some tests will be performed to see whether the participant is eligible to participate.
2. Study Treatment (45 visits): 157 weeks
If the participant is eligible, the participant will move to the treatment. The participant will be treated for 157 weeks with the study drug (ISIS
678354).
The study drug will be given at the dose of 80 mg once every 4 weeks (39 times). The study drug will be administered by using either a syringe containing the study drug that was drawn up from a vial, or an autoinjector that already contains the study drug.
The 80 mg dose of the study drug may be adjusted to 50 mg every 4 weeks (temporarily or permanently) for tolerability or safety reasons.

The participant will receive the study drug as under the skin injections in your abdomen (stomach area), thigh, or upper arm.
3. Post-treatment Follow-up (3 visits): 13 weeks

Intervention

The study drug (IISIS 678354) is expected to effectively lower triglyceride levels in patients with Familial Chylomicronemia Syndrome and may have the potential to reduce events of pancreatitis in patients with Familial Chylomicronemia Syndrome.
The study drug will be given at the dose of 80 mg once every 4 weeks (39 times). The 80 mg dose of the study drug may be adjusted to 50 mg every 4 weeks (temporarily or permanently) for tolerability or safety reasons. The study drug will be administered as under the skin injections in your abdomen (stomach area), thigh, or upper arm. The study drug will be administered by using either a syringe containing the study drug that was drawn up from a vial, or an autoinjector that already contains the study drug.

Study burden and risks

Burden: During the study, there will be 50 visits. Subjects will be treated with the study drugs once every 4 weeks for a total of 39 times. Physical and vital signs examinations, ECG (assessment electrical activity of the heart), blood and urine test will be performed. These assessments can be associated with some discomforts (e.g. taking blood can be painful, skin irritation can arise due to the electrodes of the ECG, fasting can cause faintness).Information about adverse events will be collected during the study. Participants will be asked to not consume alcohol and are encouraged to follow a low-fat diet (<20 gram fat per day) during the study. Diet and alcohol counseling will be provided.

Risk: The study drug may cause side effects. Common side effects are redness, bruising and itching at the site of injection. Those effects normally disappear within a week.
Less common side effects are:
• Mild flu-like symptoms (fever, chills, muscle aches, nausea or vomiting) could also occur during the first or second treatment. These symptoms typically resolve on its own on the same day or the day after.
• The study drug could affect the kidney. Blood and urine will be collected during the study to check these organs.

Benefit: The study drug may treat FCS but that is not certain. FCS may come back or get worse at any time during this study

Contacts

Public
Ionis Pharmaceuticals, Inc.

Gazelle Court 2855
Carlsbad CA 92010
US
Scientific
Ionis Pharmaceuticals, Inc.

Gazelle Court 2855
Carlsbad CA 92010
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Must have given written informed consent (signed and dated) and any authorizations
required by local law and be able to comply with all study requirements
2. Satisfactory completion of the ISIS 678354-CS3 index study (last dose as scheduled at Week 49) with an acceptable safety profile, per Investigator judgement
3. Willing to follow a diet comprising <= 20 g fat per day during the study
4. Satisfy the following:
a. Females: must be non-pregnant and non-lactating and either:
i. surgically sterile (e.g., tubal occlusion, hysterectomy, bilateral salpingectomy,
bilateral oophorectomy)

ii. postmenopausal (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 follicle-stimulating hormone (FSH) levels in the postmenopausal range for the laboratory involved)
iii. abstinent* or
iv. if engaged in sexual relations of child-bearing potential, agree to use a highly
effective contraceptive method from the time of signing the informed consent form until at least 30 weeks after the last dose of ISIS 678354
b. Males: Surgically sterile, abstinent* or if engaged in sexual relations with a female of
child-bearing potential, agree to use a highly effective contraceptive method from the
time of signing the informed consent form until at least 30 weeks after the last dose of
ISIS 678354
* 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
5. The following concomitant medications will be allowed if dosing regimen is expected to
remain constant through the end of the study (occasional or intermittent use of over-the-counter (OTC) medications will be allowed at Investigator*s discretion):
a. Statins, omega-3 fatty acids (prescription and OTC), fibrates, or other lipid-lowering
medications. Patients taking OTC omega-3 fatty acids should make every effort to remain on the same brand through the end of the study
b. Antidiabetic medications except glucagon-like peptide 1(GLP-1) agonist that is disallowed
c. Antihypertensive medications
d. Oral anticoagulants (e.g., warfarin, dabigatran, rivaroxaban, and apixaban) and
regular clinical monitoring is performed
e. Tamoxifen, estrogens or progestins
f. Atypical antipsychotic medications (e.g., olanzapine and clozapine)

Exclusion criteria

1. 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, including need for treatment with
medications disallowed in the index study (ISIS 678354-CS3).

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-10-2022
Enrollment:	5
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	29-04-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-06-2022

Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-12-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-01-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-04-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-05-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-07-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-08-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-12-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	16-01-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-03-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-04-2024
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
EU-CTR	CTIS2023-509029-29-00
EudraCT	EUCTR2021-003280-95-NL
ClinicalTrials.gov	NCT05130450
CCMO	NL80238.000.22