An open-label, single arm, multicenter extension study to evaluate long-term safety and tolerability of inclisiran in participants with heterozygous or homozygous familial hypercholesterolemia who have completed the adolescent ORION-16 or ORION-13 studies (VICTORION-PEDS-OLE)

Published: 27-10-2022
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This study has been transitioned to CTIS with ID 2023-507278-41-00 check the CTIS register for the current data. The primary objective of the study is to evaluate the long-term safety and tolerability of inclisiran in participants with HeFH or HoFH

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cardiac and vascular disorders congenital
Study type	Interventional

Summary

ID

NL-OMON53697

Source
ToetsingOnline

Brief title
CKJX839C12001B, VICTORION-PEDS-OLE

Condition

- Cardiac and vascular disorders congenital

Synonym
elevated LDL-C cholesterol, familial hypercholesteriolemia

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: Familial hypercholesterolemia, Inclisiran, LDL-cholesterol, Open-label extension study

Outcome measures

Primary outcome

The primary objective of the study is to evaluate the long-term safety and

tolerability of inclisiran in participants with HeFH or HoFH

(Treatment-emergent (serious) adverse events, vital signs, growth, laboratory

parameters)

Secondary outcome

To evaluate the long-term effect of inclisiran treatment on low-density

lipoprotein cholesterol (LDL-C) levels (change in LDL-C from baseline in the

feeder study to end of study (EoS))

Study description

Background summary

As the degree and duration of exposure to elevated LDL-C levels increases the atherosclerotic burden, early treatment of FH to lower LDL-C levels is vital. HeFH, guidelines recommend statins as first line drug therapy for

lipid-lowering in children, however, multiple drug therapy is often needed. In the more severe homozygous FH, maximal statin therapy is the mainstay drug treatment, often in combination with ezetimibe and other lipid-modifying therapy. However, even at the highest doses of the most efficacious statins, only modest reductions in LDL-C plasma levels of 10-25% are observed in most patients. Where available, low-density lipoprotein (LDL)-apheresis is regarded an important adjunctive treatment.
Inclisiran is a double-stranded small interfering RNA which inhibits translation of PCSK9 protein in hepatocytes. Reduced intrahepatic PCSK9 increases LDLR recycling and expression on the hepatocyte cell surface, thereby increasing LDL-C uptake and lowering LDL-C levels in the circulation.
Two currently ongoing randomized, multicenter, double-blind, Phase 3 studies (ORION-16 and ORION-13) evaluate the effects of inclisiran sodium 300mg s.c. on lowering LDL-C levels in adolescents with HeFH or HoFH. To collect long-term safety, tolerability and efficacy data and to ensure continuous treatment of participants with HeFH or HoFH upon completion of the Phase 3 studies with inclisiran, participants who complete ORION-16 or ORION-13 will be offered the opportunity to enroll in the present VICTORION-PEDS-OLE study (CKJX839C12001B) and thus continue to receive open-label treatment with 300mg s.c. inclisiran sodium. Only participants who derived a treatment benefit from inclisiran in ORION-16 and -13, per the investigator's opinion, will be included in this study.

Study objective

This study has been transitioned to CTIS with ID 2023-507278-41-00 check the CTIS register for the current data.

The primary objective of the study is to evaluate the long-term safety and tolerability of inclisiran in participants with HeFH or HoFH

Study design

This study is an open-label, single arm, multicenter, extension study to characterize long-term safety and tolerability of inclisiran and to provide access to participants with HeFH or HoFH who have completed the adolescent CKJX839C12301 (ORION-16) or CKJX839C12302 (ORION-13) studies with inclisiran and are judged by the respective study investigator to derive benefit from inclisiran treatment. Long-term efficacy of inclisiran will also be assessed.

Intervention

All participants will receive open-label, subcutaneous (s.c.) injections of inclisiran sodium 300mg.

Study burden and risks

Injections site reactions: itching, pain, rash, redness, skin color changes, sores, swelling, tenderness, or other reactions around the injection site.
Allergic reactions: these reactions can be mild or serious. common symptoms of an allergic reaction include rash, itching, skin problems, swelling of the face and throat, or trouble breathing. No general allergic reactions or signs or symptoms suggestive of general allergic reactions have been seen following administration of inclisiran in three large previous clinical studies.
Blood sampling can cause some pain and/or bruising.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

• Male and female participants with a diagnosis of HeFH or HoFH who completed

the
ORION-16 or ORION-13 studies, meaning the participant received the last dose of study
drug and completed the final study visit as per applicable protocol
• Per investigator`s clinical judgment, participant derived benefit from treatment with
inclisiran in the ORION-16 or ORION-13 studies
• Continuing current lipid-lowering therapies (such as e.g. statin and/or ezetimibe) from the
feeder study with no planned medication or dose change

Exclusion criteria

• Participants who in the feeder inclisiran ORION-16 and ORION-13 studies either screen
failed or permanently discontinued from the treatment/study for any reason or had serious
safety or tolerability issues related to inclisiran treatment
• Any uncontrolled or serious disease, or any medical, physical, or surgical condition, that
may either interfere with participation in the clinical study or interpretation of clinical
study results, and/or put the participant at significant risk
• Active liver disease defined as any known current infectious, neoplastic, or metabolic
pathology of the liver

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):	19-04-2023
Enrollment:	23
Type:	Actual

Ethics review

Approved WMO Date:	27-10-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-01-2023
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-03-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-03-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-05-2023
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	CTIS2023-507278-41-00
EudraCT	EUCTR2022-002316-23-NL
ClinicalTrials.gov	NCT05682378
CCMO	NL82579.000.22