ISRCTN88876914 https://doi.org/10.1186/ISRCTN88876914

A double-blind randomized placebo-controlled trial assessing the effects of inclisiran on clinical outcomes among people with atherosclerotic cardiovascular disease (ORION-4)

Submission date
25/06/2018

Recruitment status
No longer recruiting

Registration date
10/10/2018

Overall study status
Ongoing

Last Edited
09/12/2025

Condition category
Circulatory System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
This study aims to find out if a new cholesterol-lowering injection (called inclisiran) safely lowers the risk of heart attacks and strokes in people who have already had one of these conditions, or who have had an operation or procedure to treat blocked-up arteries.

Who can participate?
People aged at least 40 years or older in men and 55 years or older in women, who have known vascular disease (that is they have had a heart attack, a stroke, a leg artery bypass, an angioplasty or an aortic aneurysm repair)

What does the study involve?
Participants attend the study clinic 3 times in the first 5 months and every 6 months after that. At these visits, a trained researcher (usually a nurse) asks them about their health, takes a blood sample (this may not be done at every visit) and gives an injection of either inclisiran or placebo (dummy drug). Participants are asked to remain in the study for about 5 years. Wherever possible, the study team may like to stay in touch with participants after the end of the scheduled 5-year study follow-up, possibly with a simple questionnaire or phone call once or twice a year. Also, the study scientists would like to continue to get information about participant health, such as details of any admissions to hospital from NHS England (previously called NHS Digital) or other central registries after the end of the scheduled study follow-up period. This may include health information recorded throughout a person's lifetime. Participants can opt out of this if they choose.

What are the possible benefits and risks of participating?
Participants will be helping doctors and scientists improve treatment for people who have had heart attacks or strokes, or who may be at risk of having one. If successful, results from this study might help to prevent many thousands of heart attacks, strokes and bypass procedures around the world.

Most treatments have side effects, which some people may experience, and others may not. If participants experience any side effects during the study, they will be recorded so that scientists can learn from this. Participants can stop receiving the study injections at any time if they want. Inclisiran is an unlicensed drug. In a previous study including about 350 people treated with inclisiran for 6 months, about 1 in 20 people noticed some redness or soreness where the injection was given, but no other side effects were found. Inclisiran has also been given to over 1500 people in other ongoing studies, but at this stage scientists cannot rule out the possibility of side effects. All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life-threatening. Throughout the study participants will be carefully monitored for possible side effects. At every visit, the study nurse will discuss any new information about the drug.

Where is the study run from?
1. Oxford University Clinical Trial Service Unit (CTSU) (UK)
2. Brigham and Women's Hospital (USA)

When is the study starting and how long is it expected to run for?
December 2017 to December 2049

Who is funding the study?
Novartis Pharmaceuticals Corporation (USA)

Who is the main contact?
Prof. Louise Bowman
orion4@ndph.ox.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Louise Bowman

ORCID ID
https://orcid.org/0000-0003-1125-8616

Contact details
CTSU, Richard Doll Building
Roosevelt Drive
Oxford
United Kingdom
OX3 7LF
+44 (0)1865 743743
orion4@ndph.ox.ac.uk

Type(s)
Scientific

Contact name
Ms Michelle Nunn

ORCID ID
https://orcid.org/0000-0003-3195-2613

Contact details
CTSU
Nuffield Department of Population Health
University of Oxford
Richard Doll Building
Old Road Campus
Oxford
United Kingdom
OX3 7LF

Additional identifiers

ClinicalTrials.gov (NCT)
NCT03705234

Clinical Trials Information System (CTIS)
2017-005066-22

Central Portfolio Management System (CPMS)
38382

Protocol serial number
CTSU_MDCO-PCS-17-01 (CKJX839B12301)

Study information

Scientific Title
A double-blind randomized placebo-controlled trial assessing the effects of inclisiran on clinical outcomes among people with atherosclerotic cardiovascular disease (ORION-4)

Acronym
HPS-4/TIMI 65/ORION-4

Study objectives
Does inhibition of proprotein convertase subtilisin/kexin type 9 (PCSK9) synthesis with the small interfering ribonucleic acid (siRNA) inclisiran prevent cardiovascular events among people with cardiovascular disease?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Oxfordshire C Research Ethics Committee, 31/05/2018, ref: 18/SC/0243

Study design
Multicentre multinational double-blind randomized placebo-controlled parallel-group trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Myocardial infarction and stroke in people with atherosclerosis

Interventions
Current interventions as of 09/06/2023:

Screening and pre-randomization run-in:
Local investigators in UK hospitals will appoint research coordinators (usually nurses) to run local study clinics. Clinics will be run by the co-ordinator with the local investigator retaining medical oversight for the study. Potentially eligible patients will be identified (after obtaining the necessary approvals), from hospital-based computerised medical records or other NHS bodies such as NHS England.
Potentially eligible participants will be sent an invitation letter on behalf of the local investigator together with information about the study, and will be invited to attend a local study clinic and asked to call the coordinating centre in Oxford to confirm their appointment.

When they call the co-ordinating centre, trained staff will check key eligibility criteria over the phone in order to avoid a wasted visit to the clinic. Medical staff will be available to answer any questions about the study.

At their first visit (screening) they will be asked questions to assess their eligibility. After documenting written consent for the blood test, the nurse will collect a capillary blood sample and will measure a point-of-care total cholesterol level. Those with a total cholesterol level of less than 3 mmol/l are not able to continue with the study. For eligible individuals the nurse will explain the study in detail and they will be asked to sign an informed consent form. Optional consent will be sought for long-term storage of samples for genetic and, separately, for non-genetic analyses and for post-trial follow-up. Details of the participant’s cholesterol lowering medication will be collected and an injection of placebo inclisiran will be administered. The participant's Randomization appointment will be scheduled for 8 weeks time and they will be provided with a 24-hour Freephone telephone number for any trial-related queries. The participant now enters the pre-randomization run-in period of the trial.

After the screening visit each participant's general practitioner will be informed by letter of their patient's possible involvement in the study and asked to review their patient's usual cholesterol lowering medication.

Final check of eligibility and randomization:
Participants returning for their Randomization visit will be asked about any circulatory or other problems since the Screening visit, about any problems following the injection given at Screening, and if they are happy to continue in the trial. Those individuals who remain willing and eligible to continue in the trial will have a venous blood sample taken for processing for central laboratory analysis and storage. Details of all non-study treatments will be recorded and information about smoking history and alcohol intake will be sought and a quality of life questionnaire will be completed. Those who consent to continue in the trial will be assigned at random (like tossing a coin) to receive either inclisiran sodium 300 mg or placebo injection which

will then be administered by the study coordinator. The follow-up appointment in 3 months is scheduled and the participant is reminded to contact the Freephone number if they have any concerns or questions about the study.

Post-randomization follow-up at 3 months, and then 6-monthly:
Participants will be asked to attend the ORION-4 clinic initially 3 months after randomization and then 6-monthly for a median of 5 years. At each visit serious medical events will be recorded along with any changes to their concurrent medication. A venous blood sample will be taken at randomization, 3-months, 9-months and then approximately every 12-months thereafter (starting at 15-months) for processing for central laboratory analysis and storage. At each visit, participants will be asked if they are willing to continue with the study injections and, if so, the inclisiran or placebo injection will be given. If the participant is not willing to continue the study injections, the reason will be recorded. At the final study visit an assessment of quality of life will be made.

Additional "early recall" visits to clinic might be arranged for individuals who need to be reviewed before their planned appointment. This may occur in the case of symptoms possibly related to study treatment or if a participant has particular concerns.

Confirmation of reported events:
Data will be collected by the study coordinators directly onto a secure web-based case report form using specially designed and validated computer programs. Data will be stored securely on computers at the University of Oxford. All reports of possible cardiovascular events (heart attacks, strokes, revascularization procedures, etc) and other relevant serious adverse events will be independently confirmed or refuted by seeking further information about the event from the GP and hospital medical records. Participants will be flagged for mortality, cancer and other health outcomes through central registries, but will have the opportunity to opt out of this at any point during the trial.

Follow up of non-attenders:
Participants will be encouraged to continue attending study clinics even if study treatment is no longer being given. Those who are unwilling or unable to attend study clinics will be followed up by telephone if appropriate. If this is not appropriate, follow-up information will be obtained from their own doctor or central registries unless consent for this is withdrawn.

Post-trial follow-up:
Extended follow-up of all surviving randomized participants may continue for several years beyond the final study visit in order to provide valuable information on the longer term safety and efficacy of the study treatment. Data will continue to be requested from NHS England (or eDRIS in Scotland) after the final study visit and this is made clear in the Participant Information Leaflet and the Consent Form and participants will have the opportunity to opt out of this if they choose. As well as seeking long term follow-up information via routine data sources, participant questionnaires may be administered by telephone, by mail or by electronic means (e. g. secure web-based survey tools) where consent is provided for this.

Previous interventions as of 21/09/2022 to 09/06/2023:

Screening and pre-randomization run-in:
Local investigators in UK hospitals will appoint research coordinators (usually nurses) to run local study clinics. Clinics will be run by the co-ordinator with the local investigator retaining medical

oversight for the study. Potentially eligible patients will be identified (after obtaining the necessary approvals), from hospital-based computerised medical records or other NHS bodies such as NHS Digital.
Potentially eligible participants will be sent an invitation letter on behalf of the local investigator together with information about the study, and will be invited to attend a local study clinic and asked to call the coordinating centre in Oxford to confirm their appointment.

When they call the co-ordinating centre, trained staff will check key eligibility criteria over the phone in order to avoid a wasted visit to the clinic. Medical staff will be available to answer any questions about the study.

At their first visit (screening) they will be asked questions to assess their eligibility. After documenting written consent for the blood test, the nurse will collect a capillary blood sample and will measure a point-of-care total cholesterol level. Those with a total cholesterol level of less than 3 mmol/l are not able to continue with the study. For eligible individuals the nurse will explain the study in detail and they will be asked to sign an informed consent form. Optional consent will be sought for long-term storage of samples for genetic and, separately, for non-genetic analyses and for post-trial follow-up. Details of the participant's cholesterol lowering medication will be collected and an injection of placebo inclisiran will be administered. The participant's Randomization appointment will be scheduled for 8 weeks time and they will be provided with a 24-hour Freephone telephone number for any trial-related queries. Participants will be observed in the clinic for 30 minutes after the injection for any injection site reactions. The participant now enters the pre-randomization run-in period of the trial.

After the screening visit each participant's general practitioner will be informed by letter of their patient's possible involvement in the study and asked to review their patient's usual cholesterol lowering medication.

Final check of eligibility and randomization:
Participants returning for their Randomization visit will be asked about any circulatory or other problems since the Screening visit, about any problems following the injection given at Screening, and if they are happy to continue in the trial. Those individuals who remain willing and eligible to continue in the trial will have a venous blood sample taken for processing for central laboratory analysis and storage. Details of all non-study treatments will be recorded and information about smoking history and alcohol intake will be sought and a quality of life questionnaire will be completed. Those who consent to continue in the trial will be assigned at random (like tossing a coin) to receive either inclisiran sodium 300 mg or placebo injection which will then be administered by the study coordinator. The follow-up appointment in 3 months is scheduled and the participant is reminded to contact the Freephone number if they have any concerns or questions about the study.

Post-randomization follow-up at 3 months, and then 6-monthly:
Participants will be asked to attend the ORION-4 clinic initially 3 months after randomization and then 6-monthly for a median of 5 years. At each visit serious medical events will be recorded along with any changes to their concurrent medication. A venous blood sample will be taken at randomization, 3-months, 9-months and then approximately every 12-months thereafter (starting at 15-months) for processing for central laboratory analysis and storage. At each visit, participants will be asked if they are willing to continue with the study injections and, if so, the inclisiran or placebo injection will be given. If the participant is not willing to continue the study injections, the reason will be recorded. At the final study visit an assessment of quality of life will be made.

Additional "early recall" visits to clinic might be arranged for individuals who need to be reviewed before their planned appointment. This may occur in the case of symptoms possibly related to study treatment or if a participant has particular concerns.

Confirmation of reported events:
Data will be collected by the study coordinators directly onto a secure web-based case report form using specially designed and validated computer programs. Data will be stored securely on computers at the University of Oxford. All reports of possible cardiovascular events (heart attacks, strokes, revascularization procedures, etc) and other relevant serious adverse events will be independently confirmed or refuted by seeking further information about the event from the GP and hospital medical records. Participants will be flagged for mortality, cancer and other health outcomes through central registries, but will have the opportunity to opt out of this at any point during the trial.

Follow up of non-attenders:
Participants will be encouraged to continue attending study clinics even if study treatment is no longer being given. Those who are unwilling or unable to attend study clinics will be followed up by telephone if appropriate. If this is not appropriate, follow-up information will be obtained from their own doctor or central registries unless consent for this is withdrawn.

Post-trial follow-up:
Extended follow-up of all surviving randomized participants may continue for several years beyond the final study visit in order to provide valuable information on the longer term safety and efficacy of the study treatment. Data will continue to be requested from NHS Digital (or eDRIS in Scotland) after the final study visit and this is made clear in the Participant Information Leaflet and the Consent Form and participants will have the opportunity to opt out of this if they choose. As well as seeking long term follow-up information via routine data sources, participant questionnaires may be administered by telephone, by mail or by electronic means (e. g. secure web-based survey tools) where consent is provided for this.

_____

Previous interventions as of 12/08/2021 to 21/09/2022:

Screening and pre-randomization run-in:
Local investigators in UK hospitals will appoint research coordinators (usually nurses) to run local study clinics. Clinics will be run by the co-ordinator with the local investigator retaining medical oversight for the study. Potentially eligible patients will be identified (after obtaining the necessary approvals), from hospital-based computerised medical records or other NHS bodies such as NHS Digital.
Potentially eligible participants will be sent an invitation letter on behalf of the local investigator together with information about the study, and will be invited to attend a local study clinic and asked to call the coordinating centre in Oxford to confirm their appointment.

When they call the co-ordinating centre, trained staff will check key eligibility criteria over the phone in order to avoid a wasted visit to the clinic. Medical staff will be available to answer any questions about the study.

At their first visit (screening) they will be asked questions to assess their eligibility. After documenting written consent for the blood test, the nurse will collect a capillary blood sample and will measure a point-of-care total cholesterol level. Those with a total cholesterol level of less than 4 mmol/l are not able to continue with the study. For eligible individuals the nurse will

explain the study in detail and they will be asked to sign an informed consent form. Optional consent will be sought for long-term storage of samples for genetic and, separately, for non-genetic analyses and for post-trial follow-up. Details of the participant's cholesterol lowering medication will be collected and an injection of placebo inclisiran will be administered. The participant's Randomization appointment will be scheduled for 8 weeks time and they will be provided with a 24-hour Freephone telephone number for any trial-related queries. Participants will be observed in the clinic for 30 minutes after the injection for any injection site reactions. The participant now enters the pre-randomization run-in period of the trial.

After the screening visit each participant's general practitioner will be informed by letter of their patient's possible involvement in the study and asked to review their patient's usual cholesterol lowering medication.

Final check of eligibility and randomization:
Participants returning for their Randomization visit will be asked about any circulatory or other problems since the Screening visit, about any problems following the injection given at Screening, and if they are happy to continue in the trial. Those individuals who remain willing and eligible to continue in the trial will have a venous blood sample taken for processing for central laboratory analysis and storage. Details of all non-study treatments will be recorded and information about smoking history and alcohol intake will be sought and a quality of life questionnaire will be completed. Those who consent to continue in the trial will be assigned at random (like tossing a coin) to receive either inclisiran sodium 300 mg or placebo injection which will then be administered by the study coordinator. The follow-up appointment in 3 months is scheduled and the participant is reminded to contact the Freephone number if they have any concerns or questions about the study.

Post-randomization follow-up at 3 months, and then 6-monthly:
Participants will be asked to attend the ORION-4 clinic initially 3 months after randomization and then 6-monthly for a median of 5 years. At each visit serious medical events will be recorded along with any changes to their concurrent medication. A venous blood sample will be taken at randomization, 3-months, 9-months and then approximately every 12-months thereafter (starting at 15-months) for processing for central laboratory analysis and storage. At each visit, participants will be asked if they are willing to continue with the study injections and, if so, the inclisiran or placebo injection will be given. If the participant is not willing to continue the study injections, the reason will be recorded. At the final study visit an assessment of quality of life will be made.

Additional "early recall" visits to clinic might be arranged for individuals who need to be reviewed before their planned appointment. This may occur in the case of symptoms possibly related to study treatment or if a participant has particular concerns.

Confirmation of reported events:
Data will be collected by the study coordinators directly onto a secure web-based case report form using specially designed and validated computer programs. Data will be stored securely on computers at the University of Oxford. All reports of possible cardiovascular events (heart attacks, strokes, revascularization procedures, etc) and other relevant serious adverse events will be independently confirmed or refuted by seeking further information about the event from the GP and hospital medical records. Participants will be flagged for mortality, cancer and other health outcomes through central registries, but will have the opportunity to opt out of this at any point during the trial.

Follow up of non-attenders:
Participants will be encouraged to continue attending study clinics even if study treatment is no longer being given. Those who are unwilling or unable to attend study clinics will be followed up by telephone if appropriate. If this is not appropriate, follow-up information will be obtained from their own doctor or central registries unless consent for this is withdrawn.

Post-trial follow-up:
Extended follow-up of all surviving randomized participants may continue for several years beyond the final study visit in order to provide valuable information on the longer term safety and efficacy of the study treatment. Data will continue to be requested from NHS Digital (or eDRIS in Scotland) after the final study visit and this is made clear in the Participant Information Leaflet and the Consent Form and participants will have the opportunity to opt out of this if they choose. As well as seeking long term follow-up information via routine data sources, participant questionnaires may be administered by telephone, by mail or by electronic means (e. g. secure web-based survey tools) where consent is provided for this.

_____

Previous interventions:

Screening and pre-randomization run-in:
Local investigators in UK hospitals will appoint research coordinators (usually nurses) to run local study clinics. Clinics will be run by the co-ordinator with the local investigator retaining medical oversight for the study. Potentially eligible patients will be identified (after obtaining the necessary approvals), from hospital-based computerised medical records or other NHS bodies such as NHS Digital.
Potentially eligible participants will be sent an invitation letter on behalf of the local investigator together with information about the study, and will be invited to attend a local study clinic and asked to call the coordinating centre in Oxford to confirm their appointment.

When they call the co-ordinating centre, trained staff will check key eligibility criteria over the phone in order to avoid a wasted visit to the clinic. Medical staff will be available to answer any questions about the study.

At their first visit (screening) they will be asked questions to assess their eligibility. After documenting written consent for the blood test, the nurse will collect a capillary blood sample and will measure a point-of-care total cholesterol level. Those with a total cholesterol level of less than 4 mmol/l are not able to continue with the study. For eligible individuals the nurse will explain the study in detail and they will be asked to sign an informed consent form. Optional consent will be sought for long-term storage of samples for genetic and, separately, for non-genetic analyses and for post-trial follow-up. Details of the participant’s cholesterol lowering medication will be collected and an injection of placebo inclisiran will be administered. The participant's Randomization appointment will be scheduled for 8 weeks time and they will be provided with a 24-hour Freephone telephone number for any trial-related queries. Participants will be observed in the clinic for 30 minutes after the injection for any injection site reactions. The participant now enters the pre-randomization run-in period of the trial.

After the screening visit each participant's general practitioner will be informed by letter of their patient's possible involvement in the study and asked to review their patient's usual cholesterol lowering medication.

Final check of eligibility and randomization:
Participants returning for their Randomization visit will be asked about any circulatory or other problems since the Screening visit, about any problems following the injection given at Screening, and if they are happy to continue in the trial. Those individuals who remain willing and eligible to continue in the trial will have a venous blood sample taken for processing for central laboratory analysis and storage. Details of all non-study treatments will be recorded and information about smoking history and alcohol intake will be sought and a quality of life questionnaire will be completed. Those who consent to continue in the trial will be assigned at random (like tossing a coin) to receive either inclisiran sodium 300 mg or placebo injection which will then be administered by the study coordinator. The follow-up appointment in 3 months is scheduled and the participant is reminded to contact the Freephone number if they have any concerns or questions about the study.

Post-randomization follow-up at 3 months, and then 6-monthly:
Participants will be asked to attend the ORION-4 clinic initially 3 months after randomization and then 6-monthly for a median of 5 years. At each visit serious medical events will be recorded along with any changes to their concurrent medication and a venous blood sample will be taken for processing for central laboratory analysis and storage. At each visit, participants will be asked if they are willing to continue with the study injections and, if so, the inclisiran or placebo injection will be given. If the participant is not willing to continue the study injections, the reason will be recorded. At the final study visit an assessment of quality of life will be made.

Additional "early recall" visits to clinic might be arranged for individuals who need to be reviewed before their planned appointment. This may occur in the case of symptoms possibly related to study treatment or if a participant has particular concerns.

Confirmation of reported events:
Data will be collected by the study coordinators directly onto a secure web-based case report form using specially designed and validated computer programs. Data will be stored securely on computers at the University of Oxford. All reports of possible cardiovascular events (heart attacks, strokes, revascularization procedures, etc) and other relevant serious adverse events will be independently confirmed or refuted by seeking further information about the event from the GP and hospital medical records. Participants will be flagged for mortality, cancer and other health outcomes through central registries, but will have the opportunity to opt out of this at any point during the trial.

Follow up of non-attenders:
Participants will be encouraged to continue attending study clinics even if study treatment is no longer being given. Those who are unwilling or unable to attend study clinics will be followed up by telephone if appropriate. If this is not appropriate, follow-up information will be obtained from their own doctor or central registries unless consent for this is withdrawn.

Post-trial follow-up:
Extended follow-up of all surviving randomized participants may continue for several years beyond the final study visit in order to provide valuable information on the longer term safety and efficacy of the study treatment. Data will continue to be requested from NHS Digital (or eDRIS in Scotland) after the final study visit and this is made clear in the Participant Information Leaflet and the Consent Form and participants will have the opportunity to opt out of this if they choose. As well as seeking long term follow-up information via routine data sources, participant questionnaires may be administered by telephone, by mail or by electronic means (e. g. secure web-based survey tools) where consent is provided for this.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Inclisiran

Primary outcome(s)
Current primary outcome measure as of 12/08/2021:

First occurrence during the scheduled treatment period of major adverse cardiovascular event (MACE), defined as one of the following, collected with a secure web-based case report form over a median follow-up of 5 years:
1. Coronary heart disease (CHD) death
2. Myocardial infarction
3. Fatal or non-fatal ischemic stroke
4. Urgent coronary revascularization procedure

_____

Previous primary outcome measure:

Major adverse cardiovascular event, defined as occurrence of:
1. Coronary heart disease (CHD) death
2. Myocardial infarction
3. Fatal or non-fatal ischemic stroke, or
4. Urgent coronary revascularization procedure
Collected with a secure web-based case report form. Timeframe: median follow-up of 5 years

Key secondary outcome(s))
Current secondary outcome measures as of 12/08/2021:

Occurrence of the following collected with a secure web-based case report form over a median follow-up of 5 years:
1. MACE among participants recorded to be taking high-intensity statin at baseline
2. A composite of CHD death or myocardial infarction
3. Cardiovascular death

_____

Previous secondary outcome measures:

Occurrence of:
1. A composite of CHD death or myocardial infarction, or
2. Cardiovascular death
Collected with a secure web-based case report form. Timeframe: median follow-up of 5 years

Completion date
31/12/2049

Eligibility

Key inclusion criteria
History or evidence of at least one of the following:
1. Prior MI
2. Prior ischemic stroke
3. Peripheral artery disease as evident by prior lower extremity artery revascularization or aortic aneurysm repair
4. Minimum age of 40 years for men and 55 years for women (added 21/09/2022)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
40 years

Upper age limit
100 years

Sex
All

Total final enrolment
16124

Key exclusion criteria
None of the following must be satisfied (based on self-reported medical history):
1. Acute coronary syndrome or stroke less than 4 weeks before the Screening visit or during the Run-in period
2. Coronary revascularization procedure planned within the next 6 months
3. Known chronic liver disease
4. Current or planned renal dialysis or transplantation
5. Previous exposure to inclisiran or participation in a randomized trial of inclisiran
6. Current participant exclusion criterion as of 15/01/2020: Previous (within about 3 months), current or planned treatment with a monoclonal antibody targeting PCSK9, or with a drug known to be contra-indicated with inclisiran (none currently known).
Previous participant exclusion criterion: Previous, current or planned treatment with a monoclonal antibody targeting PCSK9, or with a drug known to be contra-indicated with inclisiran (none currently known)
7. Known to be poorly compliant with clinic visits or prescribed medication
8. Medical history that might limit the individual's ability to take trial treatments
for the duration of the study (e.g. severe respiratory disease; cancer or evidence of spread within approximately the last 5 years, other than nonmelanoma skin cancer; or history of alcohol or substance misuse) or may put the individual at significant risk in the opinion of the

investigator (or their authorised deputy) if he/she were to participate in the trial
9. Women of child-bearing potential, current pregnancy, or lactation
10. Current participation in a clinical trial with an unlicensed drug or device
11. Staff personnel directly involved with the study and any family member of the investigational study staff

Date of first enrolment
28/10/2018

Date of final enrolment
29/09/2023

Locations

Countries of recruitment
United Kingdom

England

United States of America

Study participating centre
CTSU
Richard Doll Building
Roosevelt Drive
Oxford
England
OX3 7LF

Study participating centre
TIMI Study Group
350 Longwood Avenue
Office Level One
Boston
United States of America
MA 02115

Sponsor information

Organisation
University of Oxford

ROR

https://ror.org/052gg0110

Organisation
Novartis (United States)

ROR
https://ror.org/028fhxy95

Funder(s)

Funder type
Industry

Funder Name
Novartis Pharmaceuticals Corporation

Alternative Name(s)
Novartis Pharmaceuticals Corp., Novartis United States, Novartis, Novartis United States of America, Novartis Corporation, Novartis US, NPC

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request. Proposals for sub-studies must be approved by the Steering Committee. The procedure for accessing the data for this study is available at https://www.ndph.ox.ac.uk/data-access. Time Frame: after the main study results have been announced and published.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No

Participant information sheet	version V2.1	27/09/2018	10/10/2018	No	Yes
Participant information sheet	version 6.0	01/09/2021	10/01/2022	No	Yes
Participant information sheet	version 7.1	21/07/2022	21/09/2022	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes