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Lowering Events in Non-proliferative retinopathy in Scotland

Submission date
19/02/2018

Recruitment status
No longer recruiting

Registration date
23/02/2018

Overall study status
Completed

Last Edited
25/06/2024

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Each year, 5,500 patients living with diabetes in Scotland need to see an NHS eye specialist because of worsening diabetic retinopathy which is when diabetes affects the inner layer of the eye. Retinopathy leads to the certification of blindness in ~1,400 patients in the UK annually, making it one of the most important causes of blindness in adults of working age. Fenofibrate is a commonly used cholesterol-lowering drug. Two large fenofibrate studies, called FIELD and ACCORD-Lipid, suggested that fenofibrate may well slow down and in some cases stop the progression of retinopathy. However, fenofibrate is not currently used for this reason and there is a need for better information. LENS is designed to provide this information. The aim of this study is to evaluate if fenofibrate therapy will slow the progression of diabetic retinopathy.

Who can participate?
Adults aged 18 and older with diabetes and moderately severe retinopathy in Scotland.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive fenofibrate tablet. Those in the second group receive a placebo (an identical dummy) tablet. All study medicine is sent to participants by post. Neither participants nor anyone they may speak to during the trial will know which tablet they are taking (fenofibrate or placebo).This study lasts for approximately six years. Participants are expected to be treated for at least three years and are only required to attend two face-to-face clinic visits, after which all follow-up is conducted using questionnaires by telephone or by computer.

What are the possible benefits and risks of participating?
There are no other direct benefits or risks from taking part in the trial. All treatments have side effects, which some people may experience and others may not. However, fenofibrate is usually well tolerated and it can be taken safely along with the vast majority of other prescribed medicines and it is hoped that the trial will confirm that taking fenofibrate regularly reduces the risk of diabetic eye disease getting worse.

Where is the study run from?
This study is being run by the University of Oxford (UK) and takes place at NHS hospitals throughout all eleven mainland Scottish health boards.

When is the study starting and how long is it expected to run for?
August 2016 to November 2023

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
1. Mrs Sarah Howard (Public)
2. Dr David Preiss (Scientific)
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2016-002656-24

ClinicalTrials.gov (NCT)
NCT03439345

Protocol serial number
CTSULENS1

Study information

Scientific Title
A randomised placebo-controlled trial of fenofibrate to prevent progression of non-proliferative retinopathy in diabetes

Acronym
LENS

Study objectives
Current study hypothesis as of 13/02/2023:
The main hypothesis is that fenofibrate therapy will slow the progression of observable diabetic retinopathy/maculopathy to referable diabetic retinopathy/maculopathy or diabetic retinopathy /maculopathy requiring laser treatment or surgical treatment compared with placebo.

Previous study hypothesis:
The main hypothesis is that fenofibrate therapy will slow the progression of observable diabetic retinopathy/maculopathy to clinically significant diabetic retinopathy/maculopathy or diabetic retinopathy/maculopathy requiring laser treatment or surgical treatment compared with placebo.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 05/12/2017, West of Scotland Research Ethics Committee (Dykebar Hospital, Grahamston Road, Glasgow, PA2 7DE, United Kingdom; +44 141 3140212; WoSREC1@ggc.scot.nhs.uk), ref: 16/WS/0149

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

Primary study design
Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied
Diabetic retinopathy

Interventions
Eligible participants initially enter an active run-in phase of 6-10 weeks.

Thereafter, participants who continue to be eligible are randomized 1:1 to one of two groups by computer-based algorithm. Those in the first group receive the fenofibrate 145mg tablets. Those in the second group receive placebo tablets.

Participants with normal renal function (eGFR >=60mL/min/1.73m2) take one tablet daily while participants with evidence of chronic kidney disease (eGFR <60mL/min/1.73m2) take one tablet every second day.

Participants are expected to be treated for at least three years and are only required to attend two face-to-face clinic visits, after which all follow-up is conducted using questionnaires by telephone or by computer.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Fenofibrate 145mg, nanoparticle formulation

Primary outcome(s)
Current primary outcome measure as of 13/02/2023:
Number of participants in whom any of the following outcomes occur during the trial: progression from having observable diabetic retinopathy/maculopathy to referable diabetic retinopathy/maculopathy, or requiring any of retinal laser therapy, vitrectomy or intra-vitreal injection of medication due to diabetic retinopathy/maculopathy.

Previous primary outcome measure:
Number of participants in whom any of the following outcomes occur during the trial: progression from having observable diabetic retinopathy/maculopathy to clinically significant diabetic retinopathy/maculopathy, or requiring any of retinal laser therapy, vitrectomy or intra-vitreal injection of medication due to diabetic retinopathy/maculopathy.

Key secondary outcome(s))
Current secondary outcome measures as of 10/02/2023:
1. Number of participants, respectively, in whom the following outcomes occur during the trial, reported separately:
1.1. Number of participants with progression of diabetic retinopathy/maculopathy to referable diabetic retinopathy/maculopathy (based on the NHS Scotland grading scheme)
1.2. Number of participants requiring retinal laser therapy for diabetic retinopathy/maculopathy (based on patient report and health records)
1.3. Number of participants requiring vitrectomy for diabetic retinopathy/maculopathy (based

on patient report and health records)
1.4. Number of participants requiring intra-vitreal injection for diabetic retinopathy /maculopathy (based on the NHS patient report and health records)
2. Any progression of diabetic retinopathy/maculopathy (based on the NHS Scotland's retinal screening grading scheme)
3. Visual acuity measured using LogMAR or Snellen chart measurement (during retinal screening visit)
4. The development of hard exudates or blot haemorrhages within 1 disc diameter of the macula (based on the NHS Scotland's retinal screening grading scheme)
5. The development of macular oedema (based on optical coherence tomography or adverse event report)
6. Visual function measured using the VFQ-25 questionnaire at baseline, approximately 2 years and final assessment
7. Quality of life measured using the EQ-5D questionnaire at baseline, approximately 2 years and final assessment
8. Total cost to the health service based on additional drug treatment and monitoring costs, and health care resource use
9. Cost-effectiveness based on incremental cost per QALY gained with fenofibrate versus placebo

Previous secondary outcome measures:
1. Number of participants, respectively, in whom the following outcomes occur during the trial, reported separately:
1.1. Number of participants with progression of diabetic retinopathy/maculopathy to clinically significant diabetic retinopathy/maculopathy (based on the NHS Scotland grading scheme)
1.2. Number of participants requiring retinal laser therapy for diabetic retinopathy/maculopathy (based on patient report and health records)
1.3. Number of participants requiring vitrectomy for diabetic retinopathy/maculopathy (based on patient report and health records)
1.4. Number of participants requiring intra-vitreal injection for diabetic retinopathy /maculopathy (based on the NHS patient report and health records)
2. Any progression of diabetic retinopathy/maculopathy (based on the NHS Scotland's retinal screening grading scheme)
3. Visual acuity measured using LogMAR or Snellen chart measurement (during retinal screening visit)
4. The development of hard exudates within 1 disc diameter of the macula (based on the NHS Scotland's retinal screening grading scheme)
5. The development of macular oedema (based on optical coherence tomography)
6. Visual function is measured using the VFQ-25 questionnaire at baseline, approximately 2 years and final assessment
7. Quality of life is measured using the EQ-5D questionnaire at baseline, approximately 2 years and final assessment
8. Total cost to the health service based on additional drug treatment and monitoring costs, and health care resource use
9. Cost-effectiveness based on incremental cost per QALY gained with fenofibrate versus placebo

Completion date
17/11/2023

Eligibility

Key inclusion criteria
1. Capable of giving informed consent
2. Diabetes Mellitus (any type except gestational diabetes)
3. Observable diabetic retinopathy/maculopathy
(defined based on NHS Scotland retinal screening grading criteria as: R1 in both eyes or R2 in one /both eyes at the most recent retinal screening assessment; or M1 in one/both eyes at any retinal screening assessment in the last 3 years)
4. Willing to either complete electronic questionnaires or conduct telephone interviews for collection of data once every 6 months

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
1151

Key exclusion criteria
Current exclusion criteria as of 16/03/2021:

1. Clinically significant DR (defined as R3 or R4 or M2 in one or both eyes)
2. History of gallbladder disease (cholecystitis, symptomatic gallstones, cholecystectomy)
3. History of acute or chronic pancreatitis
4. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >2X the upper limit of normal (ULN) according to local NHS laboratory reference range at screening visit
5. ALT or AST >2.5X ULN according to local NHS laboratory reference range at randomisation visit
6. Creatine kinase (CK) >3X ULN according to local NHS laboratory reference range at screening visit
7. CK >3X ULN according to local NHS laboratory reference range at randomisation visit
8. Estimated glomerular filtration rate (eGFR) <40mL/min/1.73m2 at screening visit
9. eGFR <30mL/min/1.73m2 at randomisation visit
10. Cirrhosis of any aetiology or any other serious hepatic disease (investigator opinion)
11. Female who is pregnant, breastfeeding, currently trying to become pregnant, or of childbearing potential and not practising birth control
12. Ongoing vitamin K antagonist (warfarin, phenindione, acenocoumarol), cyclosporine, colchicine, ketoprofen, daptomycin, fibrate therapy, or treatment with rosuvastatin 40mg daily
13. Previous myositis, myopathy or rhabdomyolysis of any cause, or diagnosed hereditary muscle disorder
14. Ongoing renal replacement therapy
15. Any previous organ transplant
16. Previous reported intolerance to any fibrate
17. Medical history that might limit the individual’s ability to take trial treatments for the duration of the study (e.g. severe respiratory disease, history of cancer within last 5 years other

than non-melanoma skin cancer; or recent history of alcohol or substance misuse)
18. Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participant at risk because of participation in the trial, or may influence the result of the trial, or the participant's ability to participate in the trial
19. LENS participants can participate in other research studies, including clinical trials. The only exclusions related to co-enrolment will be: if any other study or trial excludes co-enrolment or if the intervention being investigated in another trial has the potential to interact with fenofibrate therapy.
20. Not adherent to active run-in treatment

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Previous participant exclusion criteria as of 18/10/2019:

1. Clinically significant DR (defined as R3 or R4 or M2 in one or both eyes)
2. History of gallbladder disease (cholecystitis, symptomatic gallstones, cholecystectomy)
3. History of acute or chronic pancreatitis
4. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >2X the upper limit of normal (ULN) according to local NHS laboratory reference range at screening visit
5. ALT or AST >2.5X ULN according to local NHS laboratory reference range at randomisation visit
6. Creatine kinase (CK) >3X ULN according to local NHS laboratory reference range at screening visit
7. CK >3X ULN according to local NHS laboratory reference range at randomisation visit
8. Estimated glomerular filtration rate (eGFR) <40mL/min/1.73m2 at screening visit
9. eGFR <30mL/min/1.73m2 at randomisation visit
10. Cirrhosis of any aetiology or any other serious hepatic disease (investigator opinion)
11. Female who is pregnant, breastfeeding, currently trying to become pregnant, or of child-bearing potential and not practising birth control
12. Ongoing vitamin K antagonist (warfarin, phenindione, acenocoumarol), cyclosporine, colchicine, ketoprofen, daptomycin, fibrate therapy, or treatment with rosuvastatin 40mg daily
13. Previous myositis, myopathy or rhabdomyolysis of any cause, or diagnosed hereditary muscle disorder
14. Ongoing renal replacement therapy
15. Any previous organ transplant
16. Previous reported intolerance to any fibrate
17. Medical history that might limit the individual's ability to take trial treatments for the duration of the study (e.g. severe respiratory disease, history of cancer within last 5 years other than non-melanoma skin cancer; or recent history of alcohol or substance misuse)
18. Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participant at risk because of participation in the trial, or may influence the result of the trial, or the participant's ability to participate in the trial
19. LENS participants can participate in other research studies, including clinical trials. The only exclusions related to co-enrolment will be: if any other study or trial excludes co-enrolment or if the intervention being investigated in another trial has the potential to interact with fenofibrate therapy.
20. Not adherent to active run-in treatment

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Previous participant exclusion criteria:

1. Clinically significant diabetic retinopathy/maculopathy
(defined based on NHS Scotland retinal screening grading criteria as R3 or R4 or M2 in one/both eyes)
2. History of gallbladder disease (cholecystitis, symptomatic gallstones, cholecystectomy)
3. History of acute or chronic pancreatitis
4. ALT or AST >2X the upper limit of normal (ULN)
5. CK >3X ULN
6. Estimated glomerular filtration rate <40mL/min/1.73m2
7. Cirrhosis of any aetiology or any other serious hepatic disease
8. Female who is pregnant, breastfeeding, currently trying to become pregnant, or of child-bearing potential and not practising birth control
9. Ongoing vitamin K antagonist (warfarin, phenindione, acenocoumarol), cyclosporine, colchicine, ketoprofen, daptomycin, fibrate therapy or treatment with rosuvastatin 40mg daily
10. Previous myositis, myopathy or rhabdomyolysis of any cause, or diagnosed hereditary muscle disorder
11. Ongoing renal replacement therapy
12. Any previous organ transplant
13. Previous reported intolerance to any fibrate
14. Medical history that might limit the individual's ability to take trial treatments for the duration of the study (e.g. severe respiratory disease, history of cancer within last 5 years other than non-melanoma skin cancer; or recent history of alcohol or substance misuse)
15. Any other significant disease or disorder which, in the opinion of the Investigator, may either put the participant at risk because of participation in the trial, or may influence the result of the trial, or the participant's ability to participate in the trial

Date of first enrolment
23/07/2018

Date of final enrolment
27/07/2021

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Glasgow Royal Infirmary
NHS Greater Glasgow and Clyde
Glasgow
United Kingdom
G4 0SF

Study participating centre

Queen Elizabeth University Hospital
NHS Greater Glasgow and Clyde
Glasgow
United Kingdom
G51 4TF

Study participating centre
Princess Alexandra Eye Pavilion
NHS Lothian
Edinburgh
United Kingdom
EH3 9HA

Study participating centre
Ninewells Hospital
NHS Tayside
Dundee
United Kingdom
DD1 9SY

Study participating centre
Aberdeen Royal Infirmary
NHS Grampian
Aberdeen
United Kingdom
AB25 2ZN

Study participating centre
Monklands District General Hospital
NHS Lanarkshire
Airdrie
United Kingdom
ML6 0JS

Study participating centre
Hairmyres Hospital
NHS Lanarkshire
East Kilbride
United Kingdom
G75 8RG

Study participating centre
Forth Valley Royal Infirmary
NHS Forth Valley
Larbert
United Kingdom
FK5 4WR

Study participating centre
Queen Margaret Hospital
NHS Fife
Dunfermline
United Kingdom
KY12 0SU

Study participating centre
Victoria Hospital
NHS Fife
Kirkcaldy
United Kingdom
KY2 5AH

Study participating centre
Raigmore Hospital
NHS Highland
Inverness
United Kingdom
IV2 3UJ

Study participating centre
University Hospital Crosshouse
NHS Ayrshire and Arran
Kilmarnock
United Kingdom
KA2 0BE

Study participating centre
University Hospital Ayr
NHS Ayrshire and Arran
Ayr

United Kingdom
KA6 6DX

Study participating centre
Dumfries and Galloway Royal Infirmary
NHS Dumfries and Galloway
Dumfries
United Kingdom
DG1 4AP

Study participating centre
Borders General Hospital
NHS Borders
Melrose
United Kingdom
TD6 9BQ

Study participating centre
Wishaw General Hospital
NHS Lanarkshire
Wishaw
United Kingdom
ML2 0DP

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name

National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Current IPD sharing statement as of 10/02/2023:
Data sharing will be conducted in accordance with the Data Access Policy for the Nuffield Department of Population Health, University of Oxford (https://www.ndph.ox.ac.uk/files/about/ndph-data-access-policy-1.pdf). Sharing of data will need to comply with consent provided by participants and with regulations regarding sharing of NHS Scotland data.

Previous IPD sharing statement:
Data can be requested via the Archive Data Access Coordinator at richard.doll.archive@ndph.ox.ac.uk.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	baseline characteristics	22/02/2024	23/02/2024	Yes	No
Results article	primary outcome results	25/06/2024	25/06/2024	Yes	No
HRA research summary			28/06/2023	No	No
Protocol file	version 6.2	29/05/2020	03/09/2020	No	No
Protocol file	version 6.3	01/06/2021	30/07/2021	No	No
Protocol file	version 7.0	29/07/2022	10/02/2023	No	No
Statistical Analysis Plan	version 1.1		13/02/2023	No	No
Statistical Analysis Plan	version 1.2		04/07/2023	No	No
Statistical Analysis Plan	version 1.3	07/02/2024	09/02/2024	No	No
	Study website				

Study website	11/11/2025	11/11/2025	No	Yes