ISRCTN14333327 https://doi.org/10.1186/ISRCTN14333327

Renoprotective effects of ursodeoxycholic acid

Submission date
09/01/2017

Recruitment status
No longer recruiting

Registration date
26/01/2017

Overall study status
Completed

Last Edited
11/05/2021

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
Diabetes mellitus is a long-term condition where a person is unable to control their blood sugar levels. There are two main types of diabetes, type 1 (around 10% of cases) and type 2. In type 1 diabetes (T1DM) the immune system attacks specialised cells in the pancreas which are responsible for producing the hormone insulin (which is responsible for converting sugar in the blood to stored sugar). T1DM sufferers have a high risk of developing complications from their diabetes. Around 30-40% of diabetic patients develop kidney disease. Eventually, the kidneys are no longer able to support the body's needs (kidney failure) and so a treatment to replace the work of the failed kidneys is needed, such as dialysis (where the blood is cleaned by a machine) or transplantation of a healthy kidney. As kidney disease progresses, a protein called albumin leaks into the urine (macroalbuminuria), which affects the kidney's ability to filter the blood. Drug treatments that are now routinely used and proven to prevent kidney failure were first evaluated in patients with T1DM and macroalbuminuria. These drugs all demonstrated early reductions in macroalbuminuria which helped delay the onset of kidney failure. However these drugs do not work for everyone and so patients with T1DM and macroalbuminuria remain at high risk of kidney failure. Ursodeoxycholic acid is a chemical found in bile which is produced by the liver to help dissolve fats. It is currently approved for clinical use and treatment of gall stones and liver disease. In laboratory and animal studies Ursodeoxycholic acid reduces albuminuria and prevents the progression of kidney damage. The aim of this study is to find out whether treatment with Ursodeoxycholic acid can help protect the kidneys in T1DM patients with macroalbuminuria.

Who can participate?
T1DM patients aged between 20 and 75 who have macroalbuminuria.

What does the study involve?
Participants are randomly allocated to receive two treatments in a random order with a four week no-treatment period between the two treatments. The first treatment involves taking Ursodeoxycholic acid every day for 24 weeks and the second treatment involves taking a placebo (dummy drug) everyday for 24 weeks. At the start and end of each 24 week period, participants have a urine sample taken to measure the protein present and a blood sample to test their liver function. In addition they have an ECG test (heart rhythm monitoring test) to check their heart function.

What are the possible benefits and risks of participating?
There is no guarantee of any direct medical benefit from participating in this study. This study will be part of an effort to collect more information about a drug that may provide potential benefit to others in the future. Risks of participation in the study include potential side effects from the study drug itself, such as soft, loose stools and diarrhoea, rash, or hardening of gallstones due to build-up of calcium. There is a also a risk of pain or bruising from blood tests or skin irritation from electrodes (sticky conductive pads) used in heart rhythm monitoring.

Where is the study run from?
Diabetes Unit, Guy's Hospital (UK)

When is the study starting and how long is it expected to run for?
June 2015 to May 2022 (updated 10/05/2021, previously: May 2021)

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

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2015-003609-41

IRAS number
147826

ClinicalTrials.gov number

Secondary identifying numbers
31972, IRAS 147826

Study information

Scientific Title
The renoprotective effects of Ursodeoxycholic acid in patients with type 1 diabetes and macroalbuminuria

Acronym
UREDIA

Study objectives
The aim of this study is to evaluate if Ursodeoxycholic acid reduces albuminuria in patients with type 1 diabetes mellitus (T1DM) with residual macroalbuminuria despite established standard care.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Bloomsbury Research Ethics Committee, 19/04/2016, ref: 15/LO/1951

Study design
Randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Secondary study design

Randomised cross over trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Specialty: Diabetes, Primary sub-specialty: Both; UKCRC code/ Disease: Renal and Urogenital/ Renal failure

Interventions
Participants are randomly allocated to receive two treatments in a random order, with a 4 week wash out period of no treatment between.

Treatment one: Participants receive Ursodeoxycholic acid (500mg bid) for 24 weeks.
Treatment two: Participants receive a placebo for 24 weeks.

The total duration of participation for both treatment arms lasts for approximately 54 weeks and includes 7 visits to the study centre at Guy's Hospital London.

Intervention Type
Other

Primary outcome measure
Albumin excretion rate (AER) is measured using a standard laboratory test on three non-consecutive timed overnight urine specimens collected one week prior to visit at baseline and 24 weeks for each treatment period.

Secondary outcome measures
1. Brachial blood pressure is measured using an automated sphygmomanometer at baseline and 24 weeks
2. Central aortic blood pressure and Ao-PWV are measured using applanation tonometry… at baseline and 24 weeks
3. Glycated haemoglobin (HbA1c) is measured using blood test at baseline and 24 weeks
4. Plasma albumin is measured using blood test at baseline and 24 weeks
5. Liver function is measured using blood test at baseline and 24 weeks
6. Urine electrolytes are measured using urine test at baseline and 24 weeks
7. Endothelial and renal markers are measured using blood tests and flow mediated dilation at baseline and 24 weeks

Overall study start date
01/06/2015

Completion date
31/05/2023

Eligibility

Key inclusion criteria
1. T1DM patients aged 20 to 75 years, with residual macroalbuminuria
2. Estimated GFR ≥3 ml/min
3. Written informed consent to participate in the study prior to any study procedures
4. Ability to communicate and comply with all study procedures

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 30; UK Sample Size: 30

Key exclusion criteria
1. History of intolerance to Ursodeoxycholic acid
2. Active gastrointestinal disease (such as gall stones, inflammatory bowel disease, primary sclerosing cholangitis)
3. Non-diabetic renal disease
4. Absence of diabetic retinopathy
5. Pregnancy or lactation (female participants)
6. Insufficient understanding of the trial

Date of first enrolment
12/01/2016

Date of final enrolment
31/05/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Guy's Hospital
Diabetes Unit
Great Maze Pond

London
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SE1 9RT

Sponsor information

Organisation
King’s College London and Guy’s and St Thomas’ NHS Foundation Trust

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Sponsor type
University/education

Organisation
Guy’s and St Thomas’s NHS Foundation Trust

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Sponsor type
Hospital/treatment centre

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

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
31/05/2024

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

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