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Lixisenatide arterial stiffness trial (LAST)

Submission date
23/01/2017

Recruitment status
No longer recruiting

Registration date
01/02/2017

Overall study status
Completed

Last Edited
28/03/2019

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Type 2 diabetes mellitus (T2DM) is a long term condition where a person is unable to control their blood sugar (glucose) levels as they do not produce enough insulin to function properly (insulin deficiency), or that the body's cells don't react to insulin as they should do (insulin resistance). Diabetic kidney disease (nephropathy) develops in nearly 40% of patients with type 2 diabetes (T2DM). It is the leading cause of long-term kidney disease (chronic kidney disease; CKD) in Europe and is also associated with early heart and blood vessel disease (cardiovascular disease, CVD). The stiffness of arteries and levels of a protein called albumin in urine are key chemical indicators of heart and kidney disease. High blood sugar levels after eating are an important risk factor for developing arterial stiffness and problems with blood vessels, which can lead to CVD. A technique called aortic pulse wave velocity (Ao-PWV) is currently the best (gold standard) technique for measuring arterial stiffness in the aorta (main artery of the body). Recent studies suggest that a new class of injected drugs for the treatment of T2DM called GLP-1 agonists could potentially lower the risk of developing CVD. The aim of this study is to find out whether treatment with Lixisenatide, a GLP-1 agonist, reduces Ao-PWV and other predictors of CKD and CVD risk in patients with diabetic kidney disease.

Who can participate?
Adults aged 40 and over who have T2DM with kidney disease.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive injections of Lixisenatide 30 minutes before the first meal of the day for 24 weeks. The dose will be increased after the first two weeks. Those in the second group receive injections of a placebo (dummy drug) that looks identical to the study drug 30 minutes before the first meal of the day for 24 weeks. At the start of the study and then again after 12 and 24 weeks, participants have their Ao-PWV determined using a special scanning system as well as providing urine and blood samples which are tested in the laboratory. Blood pressure measurements are taken at the same times as well as four weeks into the study.

What are the possible benefits and risks of participating?
There are no notable benefits involved with participating. In participants who take the Lixisenatide there is a small risk of side effects such as nausea, vomiting, allergic reactions injection site and hypoglycaemia (high blood sugar).

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

When is the study starting and how long is it expected to run for?
October 2013 to January 2020

Who is funding the study?
Sanofi-Aventis (UK)

Who is the main contact?
Dr Maria Flaquer
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number
2016-001758-17

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
32501

Study information

Scientific Title
Effect of Lixisenatide on arterial stiffness in patients with diabetic nephropathy

Acronym

LAST

Study objectives
Lixisenatide may improve aortic wall structure and function (manifested by reduction in aortic pulse wave velocity (Ao-PWV)), and other predictors of chronic kidney disease (CKD) and cardiovascular disease (CVD) risk in patients with diabetic kidney disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Bloomsbury Research Ethics Committee, 17/11/2016, ref: 16/LO/1947

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

Primary study design
Interventional

Secondary study design
Randomised controlled 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
Diabetes mellitus

Interventions
Following screening visit and run phase eligible patients are randomised to one of two groups in a 1:1 ratio using a computer-generated random sequence.

Intervention group: Participants receive Lixisenatide 10 µg administered subcutaneously 30 minutes before first meal of the day which will be up titrated to 20µg after 2 weeks.

Control group: Participants receive a matched placebo administered subcutaneously 30 minutes before first meal of the day.

In both groups, the duration of treatment will be 24 weeks.

Follow up for all participants involves having Ao-PWV determined from carotid and femoral pressure waveforms obtained non-invasively by applanation tonometry using the Sphygmocor system and the provision of blood and urine samples at 12 and 24 weeks.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Ao-PWV will be determined from carotid and femoral pressure waveforms obtained non-invasively by applanation tonometry using the Sphygmocor system at baseline, 12 and 24 weeks.

Secondary outcome measures
1. Albumin excretion rate (AER) will be measured in overnight urine samples at baseline, 12 and 24 weeks
2. Augmentation index (a measurement of the pulse wave reflection on central BP) by radial artery tonometry will be taken at baseline, 12 and 24 weeks
3. ANP, a panel of cardio-renal biomarkers and AGEs will be analysed at the end of the study in serum samples collected at 12 and 24 weeks
4. Post-prandial sodium serum will be measured in serum samples at 12 and 24 weeks
5. Brachial blood pressure will be measured by an automated sphygmomanometer at baseline, 4 , 12 and 24 weeks

Overall study start date
02/10/2013

Completion date
29/01/2020

Eligibility

Key inclusion criteria
1. Written informed consent
2. Aged 40 years and over
3. Type 2 diabetes mellitus
4. Diabetic nephropathy, defined as a history of an elevated AER [albumin:creatinine ratio (ACR) ≥2.5mg/mmol in men and ≥3mg/mmol in women or AER ≥20mcg/min] or positive urine dipstick result for proteinuria or urine protein creatinine ratios (PCR)>15 mg/mmol or clinical evidence of diabetic nephropathy] in the absence of other causes of renal damage or urinary tract infections
5. Estimated glomerular filtration rate (eGFR)* ≥45 ml/min
6. On anti-hypertensive therapy with renin angiotensin system (RAS) inhibitor at a stable dose for at least 1 month prior to randomisation
7. HbA1c between 7% and 12% on anti-diabetic medications
8. Body mass index ≥30 kg/m2

Participant type(s)
Patient

Age group

Adult

Sex
Both

Target number of participants
Planned Sample Size: 120; UK Sample Size: 120

Key exclusion criteria
1. eGFR< 45 ml/min
2. Recent (within 1 year) history of CVD event
3. Uncontrolled hypertension defined as systolic BP and diastolic BP greater than 180 and 110mmHg respectively
4. Pregnancy or lactation
5. Females of child bearing potential or males able to father a child who do not agree to useing suitable methods of contraception
6. Very poorly controlled diabetes defined as HbA1c > 12%
7. Non-diabetic renal disease
8. Expected to receive an increase in the dose of RAS inhibitors during the course of study
9. History of pancreatitis
10. Active gastrointestinal (GI) or biliary disease
11. Planned major GI surgery that can/could affect upper GI function
12. History or family history of thyroid cancer or multiple endocrine neoplasia 2
13. Known allergy/intolerance to GLP-1 receptor agonist treatment, metacresol or any of the IMP or placebo components
14. Involved in current research or have recently (within 30 days) been involved in any research involving an IMP prior to recruitment
15. Insufficient understanding of the Trial or unable to comply with study requirements
16. On basal insulin and a sulphonylurea at randomisation visit
17. Already on a GLP-1 receptor agonist therapy

Date of first enrolment
30/01/2017

Date of final enrolment
30/06/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Guy's Hospital
Great Maze Pond

London
United Kingdom
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

ROR
https://ror.org/00j161312

Funder(s)

Funder type
Industry

Funder Name
Sanofi-Aventis

Results and Publications

Publication and dissemination plan
The results of the study will be reported and disseminated at international conferences and in peer-reviewed scientific journals and will follow agreement between sponsors and funder.

Intention to publish date
29/01/2021

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository (MACRO system).

IPD sharing plan summary
Stored in repository

Study outputs

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