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Trial comparing two diabetes medications (Gliclazide versus Linagliptin) on frequency of low blood sugar levels in patients with Type 2 Diabetes and chronic moderate to severe kidney disease

Submission date
02/11/2016

Recruitment status
No longer recruiting

Registration date
02/11/2016

Overall study status
Completed

Last Edited
23/06/2020

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol

Background and study aims
Type 2 diabetes mellitus (T2DM) is a growing problem worldwide. People with T2DM have difficulty controlling their blood sugar (glucose) 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). Type 2 Diabetes can lead to a range of complications, including damage to the kidneys. It is known that maintaining normal blood sugar levels with drugs helps to slow the progression of kidney disease in diabetic patients. Hypoglycaemia is a term used to describe blood sugar levels that are too low. Hypoglycaemia is not always recognised by patients and is more common in patients with kidney disease who have had diabetes for a long time. Gliclazide is currently the most commonly used diabetic drug in the UK for patients with Type 2 Diabetes with kidney disease. Over the last ten years, a new class of diabetic drugs called Gliptins (including the drug Linagliptin) have become available which have been shown to cause less hypoglycaemia than Gliclazide. The aim of this study is to find out whether treatment with Linagliptin is safer and leads to fewer episodes of hypoglycaemia than Gliclazide, in patients with Type 2 Diabetes and moderate to severe long-term kidney disease. In addition, the study aims to find out how often unrecognised hypoglycaemic episodes occur in patients on Linagliptin compared to Gliclazide, whether Linagliptin is better than Gliclazide at protecting the kidney by mechanisms independent of just lowering blood sugar levels, and which of the two drugs makes patients feel better in themselves.

Who can participate?
Adults aged between 50 and 75 years who have had T2DM for at least 10 years, have moderate to severe long-term kidney disease, and are currently being treated with Gliclazide.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group continue

taking their Gliclazide and those in the second group start taking Linagliptin instead. At the start of the study, participants in both groups have a device called a continuous glucose monitor (CGM) put in place to continuously monitor their blood sugar levels. This involves having a small sensor inserted under the skin, which measures blood sugar levels every 5 minutes over two seven day periods at the start of the study and then after eight weeks. During the two 7-day periods, patients are also asked to complete a food diary and obtain fingerprick sugar measurements using a home glucometer four times per day.
Blood and urine samples are also collected at the start of the study and after eight weeks to measure biomarkers (natural indicators) that are associated with a decline in kidney function. Participants also complete a questionnaire to see how they are feeling.

What are the possible benefits and risks of participating?
Participants benefit from receiving their test results and explanations at the end of the study so they have more information about their diabetic control. There is a risk of minor bruising at the site where blood samples were taken, occasional minor bleeding and bruising when the CGM sensor is inserted under the skin, occasional irritation from the adhesive dressing used to secure the sensor to the skin, and occasional discomfort from the fitting and wearing of the CGM. Sometimes, the sensor may become dislodged and sound an alarm. Any changes to diabetic medication carries a small risk of affecting diabetic control, however, this will be closely monitored to minimise that risk.

Where is the study run from?
1. Hammersmith Hosptial (UK)
2. St Mary's Hospital (UK)

When is the study starting and how long is it expected to run for?
August 2014 to July 2018

How long will the trial be recruiting participants for?
Boehringer Ingelheim Ltd (UK)

Who is the main contact?
Mr Thomas Walters
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2015-002309-12

Protocol serial number
30706

Study information

Scientific Title
A randomised controlled trial of the sulfonylurea Gliclazide and the DPP-4 inhibitor Linagliptin On the frequency of hypOglyCaemia amOng patients with Type 2 DiabeteS and chronic kidnEy disease (CKD) stage 3b and 4

Acronym
GLOOCOSE

Study objectives
1. Linagliptin is associated with fewer episodes of hypoglycaemia than Gliclazide in patients with Type 2 Diabetes and moderate to severe kidney disease
2. Linagliptin reduces biochemical markers in the blood and urine associated with deteriorating kidney function and kidney disease progression
3. Patients feel better when they are taking Linagliptin, compared to Gliclazide

Ethics approval required
Old ethics approval format

Ethics approval(s)
London Brent Research Ethics Committee, 30112015, ref: 15/LO/1548

Primary study design
Interventional

Study design
Single-centre open-label unblinded randomised controlled Phase IV trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Renal disorders, Primary sub-specialty: Renal disorders; UKCRC code/ Disease: Renal and Urogenital/ Other disorders of kidney and ureter, Renal and Urogenital/ Other disorders of kidney and ureter

Interventions

Participants will undergo automated computer randomisation (using the InForm study database) to either continuing with their current treatment and dose of oral Gliclazide, or switching to oral Linagliptin 5 mg daily for eight weeks. If they were also taking Metformin, then they will continue on this. Prior to randomisation, study participants will be fitted with a continuous glucose monitor (CGM) which will capture and record interstitial glucose readings for seven days, and allow assessment of overall glycaemic control. They will also be taught to perform capillary glucose readings using a home glucose monitor (to allow CGM calibration), and complete food diaries over the week.

Eight weeks after randomisation, they will repeat this process for another 7-day period. Blood and urine samples will be obtained from study participants before and after randomisation for analysis of renal function, full blood count, HbA1c for glycaemic control, urinary albumin excretion and renal biomarkers MCP-1 and TGF-beta 1. Study patients will also be required to complete the Diabetes Treatment Satisfaction Questionnaire (DTSQ) at baseline and 8 weeks post-randomisation.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
1. Linagliptin 2. Gliclazide

Primary outcome(s)
Overall glycaemic control and percent of time spent in hypoglycaemia will be assessed using data captured on the Medtronic iPro2 Continuous Glucose Monitor over a two 7 day periods (a minimum of continuous 48 hours of CGM monitoring) and home capillary blood glucose monitoring at Visit 1 (baseline, before randomisation) and Visit 4 (7 weeks after randomisation).

Key secondary outcome(s)
1. Serum and Urinary markers of inflammation and fibrosis will be analysed by measuring urinary albumin excretion and serum and urinary MCP-1 and TGF-beta 1 at Visit 2 (randomisation visit, 1 week after baseline visit) and Visit 5 (final study visit, 8 weeks after randomisation)
2. Treatment satisfaction will be measured using the Diabetes Treatment Satisfaction Questionnaire (DTSQ) at Visit 2 (randomisation visit, 1 week after baseline visit) and Visit 5 (final study visit, 8 weeks after randomisation)

Completion date
31/07/2018

Eligibility

Key inclusion criteria
1. Type 2 Diabetes of 10 years or more duration
2. Age between 50 years and 75 years
3. eGFR 15 to 45 ml/min/1.73m2
4. HbA1c < 65 mmol/mol (< 8%)

5. Taking Gliclazide (with or without Metformin)
6. Stable diabetic control for the last 2 months prior to randomisation
7. Individuals who understand adequate written and verbal English

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
23

Key exclusion criteria
1. Type 1 Diabetes
2. Currently on insulin, pioglitazone, other dipeptidylpeptidase-4 inhibitors, glucagon-like peptide-1 receptor agonists
3. Immunosuppressive therapy (excluding inhaled steroids) within the previous 6 months
4. Pregnant or lactating women
5. Malignancy or other life threatening illness
6. Inability to give informed consent

Date of first enrolment
17/06/2016

Date of final enrolment
16/06/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Hammersmith Hospital
Imperial College Healthcare NHS Trust
Renal Research Office
2nd Floor Hammersmith House
Du Cane Road

London
United Kingdom
W12 0HS

Study participating centre
St Mary's Hospital
Imperial College Healthcare NHS Trust
Imperial Clinical Respiratory Research Unit (ICRRU)
1st Floor, Mint Wing
Praed Street
London
United Kingdom
W2 1NY

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Industry

Funder Name
Boehringer Ingelheim Ltd

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 from Thomas.Walters@imperial.nhs.uk

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		01/06/2020	01/06/2020	No	No
Basic results			23/06/2020	No	No
HRA research summary			28/06/2023	No	No