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The effect of lixisenatide in type 1 diabetes

Submission date
03/04/2014

Recruitment status
No longer recruiting

Registration date
03/04/2014

Overall study status
Completed

Last Edited
21/06/2019

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Lixisenatide has been developed as an drug for diabetes and has been shown to improve blood sugar control in people with type 2 diabetes. This study aims to find out whether a daily injection of lixisenatide, along with prescribed insulin treatment, can improve blood sugar control in people with type 1 diabetes. The study will also find out if there is a difference between participants who have low insulin production from the pancreas and those who do not have insulin production from the pancreas. Part A of this study aims to find out a safe dose of insulin when given with lixisenatide, so that the participants do not experience a higher than normal frequency of low blood sugar events. The Part B is aiming to see whether there is an effect on blood sugar levels, especially after meals, when a daily injection of lixisenatide is added to a participants usual insulin treatment.

Who can participate?
People aged 18-70 years who have had type 1 diabetes for at least 12 months and use insulin injections to control their disease can take part.

What does the study involve?
The Part A study will last about 8 days for each participant and will involve a maximum of 7 Churchill Hospital visits and 5 telephone calls from our research team. Each participant will receive lixisenatide daily for up to 4 days alongside their usual insulin medication. The Part B study will last about 16 weeks for each participant and will involve a maximum of 13 Churchill hospital visits and 6 telephone calls from our research team. There will be two different treatment periods each lasting for 4 weeks with an additional 4 weeks in between when each participant will take insulin alone (the washout period). Participants will receive lixisenatide for 4 weeks and a matching dummy or placebo drug for the other 4 weeks. Neither the study team nor the participants will know which is which.

What are the possible benefits and risks of participating?
There are no direct benefits to the participant for taking part in this exploratory study. However, the results may help researchers find the correct dose for the meal-time insulin when used with lixisenatide for the next part of the study. This study may lead to future large-scale studies and lixisenatide may become an additional treatment for patients with type 1 diabetes. Reported side effects of lixisenatide include nausea and vomiting, loss of appetite and weight loss. Most side effects settle within days of starting the medication. When lixisenatide is used with insulin

there may be a small risk of low blood sugar. The participants insulin dose will be reduced while they take the study drug to minimise this risk. The dose used in the daily injection is the same as used in type 2 diabetes. The participants health will be monitored closely during the study and the study medication would be stopped should there be any cause for concern.

Where is the study run from?
Churchill Hospital, Oxford, UK.

When is the study starting and how long is it expected to run for?
May 2014 to June 2016

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

Who is the main contact?
Dr Chitrabhanu Ballav (Principal Investigator)

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2013-002259-14

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
15724

Study information

Scientific Title

The effect of lixisenatide in type 1 diabetes: a randomised controlled trial

Acronym
LIXI

Study objectives
The study will take place in two parts (Parts A and B): The principal question of the Part A trial is to assess the amount of mealtime (prandial) insulin dose reduction that will avoid hypoglycaemic episodes (low blood sugar levels) when taken alongside a GLP1 receptor agonist called lixisenatide at a dose of 10 µg/day. The principal question of the Part B trial is to determine whether adding lixisenatide to basal bolus insulin (combination of long-acting insulin once a day, called basal, with short-acting insulin with meals, called bolus) significantly improves glycaemic (blood sugar) control during the 3-hour post-prandial period (i.e., following a meal) compared to basal bolus insulin and a 'dummy' or placebo injection.

Ethics approval required
Old ethics approval format

Ethics approval(s)
13/LO/1656; First MREC approval date 10/01/2014

Study design
Randomised; Interventional; Design type: Treatment

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
Topic: Diabetes; Subtopic: Type 1 ; Disease: Diabetic Control

Interventions
Part A study is open-label, without randomisation. All participants will receive 10 micrograms lixisentatide for up to 4 days and be followed up for 28 days after the last dose of the lixisenatide. Part B is a double-blinded trial. Two four-week treatment regimens will be applied in randomised order to participants as follows:
1. Lixisenatide 10 micrograms for 2 weeks
2. Lixisenatide 20 micrograms for 2 weeks
3. Washout period of 4 weeks

4. Matching placebo 10 micrograms for 2 weeks
5. Matching placebo 20 micrograms for 2 weeks
Neither the participant nor the trial team will know the treatment order. The participant will be followed up for 28 days after their last dose of lixisenatide (or matching placebo)

Intervention Type
Other

Phase
Phase II

Primary outcome measure
Lixisenatide effect on 3 hr post-prandial Continuous Glucose Monitoring readings compared to placebo; Timepoint(s): Part B trial.

Secondary outcome measures
HbA1c, insulin dose and glucagon change after standard mixed meal and insulin-induced hypoglycaemia; Timepoint(s): Following 4 weeks' compliance with study medication.

Overall study start date
02/05/2014

Completion date
30/06/2016

Eligibility

Key inclusion criteria
Inclusion criteria as of 08/02/2016:
1. Has provided written informed consent
2. Type 1 diabetes
3. Diabetes duration for at least 12 months
4. Age 18-70 years inclusive (upper age limit specified for clinical safety as there is limited experience of using lixisenatide beyond 75 years
5. Basal-Bolus insulin regimen
6. HbA1c between 7.0% and 10.0% (inclusive)
7. Stable insulin dose (within 20%) over 3 months prior to recruitment. Patients on low doses of insulin who have had a change of insulin dose by >20% over the preceding 3 months may be included at the discretion of the Principal Investigator
8. BMI < 35 kg/m2
9. For the C-peptide positive group: random or fasting C-peptide = 0.1 nmol/l. If clinically indicated, screen negative for mutations in HNF1A, HNF4A or GCK genes (indicative of MODY, maturity onset diabetes of the young). For the C-peptide negative group: random or fasting C-peptide <0.01 nmol/l with accompanying glucose >4 mmol/l

Original inclusion criteria:
1. Has provided written informed consent
2. Type 1 diabetes
3. Diabetes duration for at least 12 months
4. Insulin treatment since the diagnosis of diabetes
5. Age 18-65 years (upper age limit specified for clinical safety as there is limited experience of

using lixisenatide beyond 65 years)
6. Basal-Bolus insulin regimen
7. HbA1c between 7.0% and 9.0% (inclusive)
8. Stable insulin dose (within 20%) over 3 months prior to recruitment. Patients on low doses of insulin who have had a change of insulin dose by >20% over the preceding 3 months may be included at the discretion of the Principal Investigator
9. BMI < 30 kg/m2
10. For the C-peptide positive group: random or fasting C-peptide = 0.1 nmol/l. If clinically indicated, screen negative for mutations in HNF1A, HNF4A or GCK genes (indicative of MODY, maturity onset diabetes of the young). For the C-peptide negative group: random or fasting C-peptide <0.02 nmol/l with accompanying glucose >4 mmol/l

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
Planned Sample Size: 33; UK Sample Size: 33; Description: All participants will be patients with type 1 diabetes. There will be no controls in this trial.

Total final enrolment
27

Key exclusion criteria
1. Type 2 diabetes
2. Maturity Onset Diabetes of the Young (MODY)
3. Pregnancy or women of childbearing age without adequate contraception
4. Women who are breastfeeding
5. Major psychiatric disease including diagnosed eating disorders, history of drug or alcohol abuse
6. Renal impairment (eGFR ≤ 50 ml/min)
7. Abnormal liver function tests (> 1.5 x upper limit of the normal range)
8. Have high blood pressure (>180 mmHg systolic or >100 mmHgdiastolic)
9. Known ischaemic heart disease or heart failure
10. History of stroke
11. Patient has received any investigational drug within 30 days prior to screening
12. Oral steroid treatment 30 days prior to randomisation
13. Known malignancy or any other condition or circumstance, which, in the opinion of the investigator, would affect the patients ability to participate in the protocol
14. Non-English speakers will be excluded due to the nature and complexity of the

hypoglycaemic clamp methodology
15. Known allergy to the drugs or any of the components
16. Severe hypoglycaemia requiring third party intervention on more than one occasion in the preceding 12 months
17. (For Part B trial) took part in the lixisenatide prandial dose-finding Part A trial
18. Felt to be unsuitable to participate in the trial in the opinion of the Principal Investigator
19. Currently taking domperidone, metoclopramide or warfarin

Date of first enrolment
02/05/2014

Date of final enrolment
04/01/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Churchill Hospital
Oxford
United Kingdom
OX3 7LJ

Sponsor information

Organisation
University of Oxford (UK)

Sponsor details
Research Services
Clinical Trials and Research Governance
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Churchill Hospital
Headington
Oxford
England
United Kingdom
OX2 6HE

Sponsor type
University/education

Website
http://www.admin.ox.ac.uk/researchsupport/ctrg/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
Sanofi Aventis (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			21/06/2019	No	No
HRA research summary			28/06/2023	No	No