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Randomised, controlled, parallel-group prospective study to investigate the clinical effectiveness of early insulin treatment in patients with Latent Autoimmune Diabetes in Adults

Submission date 27/03/2007	**Recruitment status** No longer recruiting
Registration date 10/05/2007	**Overall study status** Completed
Last Edited 04/10/2018	**Condition category** Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2006-004662-14

IRAS number

ClinicalTrials.gov number
NCT00776607

Secondary identifying numbers
EudraCT 2006-004662-14 AND S06 GenMed601

Study information

Scientific Title
Randomised, controlled, parallel-group prospective study to investigate the clinical effectiveness of early insulin treatment in patients with Latent Autoimmune Diabetes in Adults

Acronym
LIT (LADA Insulin Trial)

Study objectives
Treatment for Latent Autoimmune Diabetes in Adults (LADA) should be that used for type 1 diabetes (insulin) rather than type 2 diabetes (tablets) in order to maintain glucose control (HbA1c) and natural insulin production (C-peptide).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Multi-Centre Research Ethics Committee (MREC) for Wales, 22/02/2007, ref: 07/MRE09/8

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

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
Latent autoimmune diabetes in adults

Interventions

1. Treatment group one - insulin:
Patients will be given advice on diet, exercise and lifestyle and will be started on NovoMix 30, one dose of 6 U at the evening/main meal. Dose will be adjusted in increments of 2 - 6 U depending on fasting glucose level. Adjustment of breakfast and/or evening meal dose (i.e. evening dose for pre-breakfast glucose and morning dose for pre evening meal glucose) will be performed once a week as follows:

a. Less than 3.0 Mmol/l or severe hypoglycaemia: -4 U
b. 3.1 - 4.4 Mmol/l: -2 U
c. 4.5 - 6.0 Mmol/l: No change
d. 6.1 - 7.8 Mmol/l: +2 U
e. 7.9 - 10.0 Mmol/l: +4 U
f. Greater than 10.0 Mmol/l: +6 U

When total dose equals 16 U patient will be started on 4 U with breakfast and continue with 16 units with evening meal. Breakfast and/or evening meal dose will be adjusted where necessary at increments of 2 - 6 U depending on fasting and/or pre-evening meal glucose level. Patient needs to keep a daily diary of insulin doses taken.

2. Treatment group two - tablets:
a. Step one: patients not treated with tablets will be given a three months trial of lifestyle modification including advice on diet, exercise and smoking. If HbA1c remains above 7% patients will progress to step two. Patients will be progressed to step two if their General Practitioner (GP) has already put them on metformin (put in at number of metformin tables that GP has recommended) or sulphonylurea or if their baseline HbA1c is above 8% (patients will start on one 500 mg tablet per day). This means that sulphonylurea will be discontinued in all patients. Patients on step one will be progressed to step two before the three-month period if they have already had a three-month period of diet before starting the study AND during phone contact they report to be symptomatic (thirst, fatigue, polyuria) and unwell. In these cases, patients may be invited to attend clinic before the three-month period to be given metformin
b. Step two: lifestyle modification and Metformin. If the patient has an HbA1c of 7% - 7.5% they start on 500 mg x 1 per day for the next three months. If the HbA1c is 7.6% - 8.0% they would start the first week on 500 mg x 1 day and then for the remaining period of the three months will take 500 mg x 2 per day. If the HbA1c is above 8.0% then patient will be on 500 mg x 3 per day. This will be titrated at the rate of 500 mg x 1 for the first week, 500 mg x 2 for the second week and 500 mg x 3 for the remaining time of the three-month period. If unable to tolerate metformin then the participant will be given Glucophage SR and if unable to tolerate this they will then progress to Step three. If HbA1c remains above 7% then those on one tablet per day will be moved to two tablets per day, those on two tablets per day will be moved to three tablets per day, those on three tablets per day will be move to maximum dose of 2 g per day. If after three months the HbA1c is above 7% even with maximum dose, then progress to Step three. If during telephone contact the patient reports symptoms then they may be titrated up. In summary, patients will be have their HbA1c evaluated every three months and will be titrated accordingly
c. Step three: lifestyle modification and Glitazone (Roseglitazone). Patients with an HbA1c of above 7% will be given 4 mg once per day for three months. If after a three-month period the HbA1c remains above 7% then titrate to maximal dose of 4 mg twice per day with or without Metformin. If HbA1c remains above 7% for an additional three months then move to step four. Therefore, glitazone monotherapy will be used if Metformin intolerant otherwise glitazone will be added to the metformin (as per standard practice)
d. Step four: lifestyle modification and insulin therapy (oral agents will be stopped). Titration will

be based on fasting blood glucose level. The initiation of insulin will the same as for the insulin arm and will follow the protocol detailed above

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Metformin, glitazone, insulin

Primary outcome measure
To examine the effect of standard treatment for type one (insulin [NovoMix 30] therapy) compared to standard treatment for type two diabetes (tablets) on:
1. Change in fasting serum C-peptide level over 24 months in patients with LADA, and
2. Change in HbA1c level over 24 months in patients with LADA

Secondary outcome measures
To assess the effect of standard type one treatment (insulin) on:
1. Average number of times the fasting plasma glucose level is above 8 mmol/l (141 mg/dl)
2. Quality of life
3. Proportion of patients with insulin dependence (as judged by C peptide level)
4. GAD antibody level
5. Homeostasis Model Assessment (HOMA)
6. Adverse events (particularly hypoglycaemic events)
7. Weight/blood pressure/total cholesterol and inflammatory markers in LADA patients compared to standard type two diabetes treatment

Overall study start date
01/06/2007

Completion date
01/06/2011

Eligibility

Key inclusion criteria
1. Male, non-fertile female (i.e., post menopausal, post hysterectomy, or sterilised by tubal ligation) or female of childbearing potential using a medically approved birth control method
2. The patient has a diagnosis of diabetes mellitus according to World Health Organisation (WHO) classification
3. The patient has a positive Glutamic Acid Decarboxylase (GAD) antibody test of 101 units or more on two separate occasions
4. Aged 18 years or more
5. Not on insulin within one month of diagnosis
6. Written informed consent to participate in the study
7. Ability to comply with all study requirements

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
210

Key exclusion criteria
1. Pregnant or breast-feeding females and females who plan pregnancy or breast-feeding during the course of the study
2. A history of:
2.1. Diabetes that is a result of pancreatic injury, or secondary forms of diabetes, e.g., Cushing's syndrome and acromegaly
2.2. Acute metabolic diabetic complications such as ketoacidosis or hyperosmolar state (coma) within the past six months
3. Acute infections, which may affect blood glucose control within four weeks prior to visit one
4. Malignancy including leukaemia and lymphoma (not including basal cell skin cancer) within the last five years
5. The patient has a known immune deficiency from any disease, or a condition associated with an immune deficiency
6. The patient is receiving immunosuppressive or immunomodulating agents or cytotoxic therapy, or any medication that, in the opinion of the site investigator, might interfere with the study
7. Any of the following significant laboratory abnormalities:
7.1. Patients with severe renal failure as defined previous renal transplant or currently having renal dialysis or Glomerular Filtration Rate (GFR) less than 30
7.2. Clinically significant laboratory abnormalities, confirmed by repeat measurement, that may interfere with the assessment of safety and/or efficacy of the study drug, other than hyperglycaemia and glycosuria at visit one
7.3. Severe ketonuria (+++ on urine sticks testing; ++ on repeated urine sticks testing)
8. The patient is a known or suspected drug abuser
9. The patient has chronic hepatitis or liver cirrhosis, or any other chronic liver disease
10. The patient is known to test positive for hepatitis B antigens or hepatitis C antibodies
11. The patient is known to test positive for Human Immunodeficiency Virus (HIV) antibodies
12. The patient has any significant diseases or conditions, including psychiatric disorders and substance abuse that, in the opinion of the site investigator, are likely to affect the patient's response to treatment or their ability to complete the study
13. The patient has chronic haematological disease
14. The patient has had a severe blood loss (greater than or equal to 400 mL, e.g., blood donation) within two months before the first dosing of the study medication
15. The patient has known proliferative retinopathy
16. Patient has had stage three to four heart failure
17. The patient is participating in another research study which may affect the results of this trial

Date of first enrolment
01/06/2007

Date of final enrolment
01/06/2011

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
School of Medicine
Swansea
United Kingdom
SA2 8PP

Sponsor information

Organisation
Swansea NHS Trust (UK)

Sponsor details
Central Clinic
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Sponsor type
Hospital/treatment centre

Website
http://www.swansea-tr.wales.nhs.uk/

ROR
https://ror.org/04zet5t12

Funder(s)

Funder type
Industry

Funder Name
Novo Nordisk Ltd (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?
Protocol article	protocol	24/07/2008		Yes	No
Results article	results	01/07/2011		Yes	No