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Advantage of using Glucophage® SR (a Metofrmin) in non-overweight patients with type-1 Diabetes to improve their glucose control

Submission date	Recruitment status	[X] Prospectively registered
14/09/2010	Stopped	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
17/09/2010	Stopped	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
03/06/2015	Nutritional, Metabolic, Endocrine	[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title

Effectiveness of Glucophage® SR as an adjunct to insulin in improving glycaemic control, without increasing the episodes of hypoglycaemia, in non-overweight patients with type 1 diabetes

Study objectives
To study the improvement in glycaemic control, without increasing the episodes of hypoglycemia, following the addition of Glucophage® SR (Merck Serono) as an adjunct to insulin in non-overweight patients with type 1 diabetes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval pending

Study design
Double-blind randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type 1 diabetes

Interventions
1. Screening Visit:
At the 'screening visit' patients will attend in fasting state (due to C-peptide levels collection on this visit) and be asked to sign a consent form and data will be collected on age, sex, height, weight, body mass index (BMI), duration of diabetes, total daily insulin dose and incidence of hypoglycemia. Blood samples will be taken for fasting blood glucose, fasting C-peptide levels, HbA1c, urea and electrolytes (U&E) and liver function tests (LFTs). A complete physical examination and fundoscopy will be done. If available, record of any recent Diabetic retinopathy screening or laser eye treatment will be sought from patient's hospital notes. Patients will be given education on how to do home glucose monitoring (HGM), will be given a HGM booklet and a glucometer. Patients will be advised to do HGM (pre-breakfast, pre-lunch, pre-evening meal and pre-bed) three days prior to every visit. In addition, patients will be asked check the blood glucose whenever they feel the symptoms of hypoglycemia (defined as capillary blood glucose < 4.0mmol/L with or without symptoms) and record it with date and time.

2. Run-in period:
Patients will receive education about study and an assessment of patient's ability to comply with the protocol will be made.

3. Randomisation:
Patients will attend in a non-fasting state and data will be collected on weight, body mass index (BMI), total daily insulin dose and incidence of hypoglycemia. Blood samples will be taken for HbA1c, U&E and LFTs. Records of hypoglycemia during 'run-in period' and HGM 3 days prior to randomization visit will be checked. Insulin dosages will be adjusted as required. Patients will be

randomized (double blind) to receive:
3.1. Glucophage® SR 5..mg once daily for 1 week, then twice daily for 6 months
3.2. Placebo

4. Intervention period:
Patients will attend at week-1 (day-7), week-2 (day-14) and week-3 (day-21). At each of these three visits the record of HGM will be reviewed and insulin dosages will be titrated as required. In addition, at visit week-1 (day-7) the Glucophage® SR will be increased to 500mg twice daily (BD) {or equivalent in the placebo arm}. On each visit the tolerability and side effects of Glucophage® SR will be evaluated and recorded. Patients can continue in the study only if they are able to tolerate a minimum dose of Glucophage® SR 500mg twice daily.
Following the visit on week-3 (day-21), there will be a total of 6 visits every month from the date of randomisation visit. At each of these visits patients will attend in a non-fasting state and data will be collected on weight, body mass index (BMI), total daily insulin dose and incidence of hypoglycemia. Blood samples will be taken for HbA1c, U&E and LFTs. Records of hypoglycemia during every visit and HGM 3 days prior to every visit will be checked. Insulin dosages will be adjusted. At the end of study visit (1 week after final monthly visit) blood pressure and pulse will be checked and physical examination will be done to ensure the patient is doing well. Patients will be switched back to their pre-study medications

5. Follow up visit:
During the follow up appointment in Diabetes clinic, approx 2 months post intervention, study results will be discussed and if the results are found favourable for Glucophage® SR as an adjunct to insulin in this group of patients, the patients will be offered to start this combination treatment

Updated 03/06/2015: The trial has been stopped due to poor recruitment and an interim analysis that suggested no benefit in continuing the trial.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Glucophage® SR (metformin [slow releasing formulation])

Primary outcome(s)
Improvement in glycaemic control as a result of addition of Glucophage® SR compared with placebo. Assessed by measurement of HbA1c at screening, baseline and 1, 2, 3, 4, 5 and 6 months.

Key secondary outcome(s))
1. Improvement in number of episodes of hypoglycemia in Glucophage® SR arm of study
2. Reduction in insulin dose in Glucophage® SR arm of the study
All outcomes assessed at screening, baseline and 1, 2, 3, 4, 5 and 6 months.

Completion date
01/11/2012

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. Male or female, Aged > 18 years
In addition, patients should fulfil all the following criteria at the randomisation visit:
2. Type-1 Diabetic patients with C-peptide negative result at screening visit (defined as C-peptide concentration < 0.18nmol/L at a time when blood glucose level is > 5.0mmol/L)
3. Suboptimal glycaemic control (HbA1c 7.5% to 8.5% at screening visit) with or without history of mild hypoglycemia (defined as hypoglycemia not affecting cognitive function and not requiring third party intervention for reversal)
4. History of previous attempts to improve glycaemic control resulting in hypoglycemic episodes (history from hospital medical notes or directly from patients)
5. History of Diabetes for > 1 year
6. BMI 21 to 27
7. Willing and able to comply with the study protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Previous History of myocardial infarction (MI) (in last 12months)
2. Congestive Cardiac Failure (New York Heart Association [NYHA] class III or IV)
3. Chronic kidney disease with estimated Glomerular Filtration Rate (eGFR) < 45mL/minute/1.73m2
4. Abnormal Alanine Aminotransferase (ALT) (> 3fold at baseline)
5. Hypoglycaemia symptoms unawareness
6. History of hypoglycemic episodes requiring 3rd party assistance for reversal
7. Uncontrolled Hypertension (BP > 180/100mmHg)
8. Pregnant OR likelihood of pregnancy during the study
9. Females who are breast feeding
10. Proliferative Diabetic retinopathy and / or laser treatment in last 12 months
11. History of Diabetic ketoacidosis, lactic acidosis and gasteroparesis
12. Previous or current treatment with metformin / Glucophage® SR
13. History of irritable bowel syndrome.
14. Previous intolerance to metformin or Glucophage® SR

15. History of weight loss in last 6 months
16. History of allergic or hypersensitivity reaction to Glucophage® SR or any insulin

Date of first enrolment
01/11/2010

Date of final enrolment
01/11/2012

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
West Wales Hospital
Carmarthen
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SA31 2AF

Sponsor information

Organisation
West Wales Hospital (UK)

ROR
https://ror.org/01cs14q41

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
West Wales Hospital (UK) - Diabetes Research fund

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration