

Pancreatic beta-cell dysfunction REStorEd by Rosiglitazone and Valsartan Effects: a 52-week randomised controlled factorial study in subjects with impaired fasting glucose and/or impaired glucose tolerance

Submission date

28/09/2006

Recruitment status

No longer recruiting

☒ Prospectively registered

☐ Protocol

Registration date

28/09/2006

Overall study status

Completed

☐ Statistical analysis plan

☒ Results

Last Edited

08/07/2013

Condition category

Nutritional, Metabolic, Endocrine

☐ Individual participant data

Plain English summary of protocol

Not provided at time of registration

Study website

<http://www.trialregister.nl>

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N/A

Study information

Scientific Title

Acronym

PRESERVE TRIAL

Study objectives

Type two diabetes is caused by progressive beta-cell dysfunction against a background of obesity and insulin resistance in susceptible individuals.

Peroxisome Proliferator-Activated Receptor (PPAR) gamma-mediated mechanisms are involved in the regulation of important processes that may protect the pancreatic beta-cell. Local pancreatic and systemic activation of the Renin-Angiotensin System (RAS), as frequently observed in people with obesity/insulin resistance, may be harmful to the pancreatic beta-cell causing beta-cell dysfunction and beta-cell apoptosis.

Treatment of subjects at high risk to develop type two diabetes, including those with impaired fasting glucose and/or impaired glucose tolerance (with/without a family history of diabetes) with a PPAR gamma agonist and/or an angiotensin II receptor blocker may improve beta-cell function.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics approval received from the local medical ethics committee

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

Health condition(s) or problem(s) studied

Impaired glucose metabolism

Interventions

Participants will be randomised into one of the following four treatment groups for a 52-week intervention:

1. Rosiglitazone 8 mg daily and valsartan-placebo
2. Valsartan 320 mg daily and rosiglitazone-placebo
3. Rosiglitazone 8 mg daily and valsartan 320 mg daily
4. Rosiglitazone-placebo and valsartan-placebo

Further information as of 10/07/12: The decision was made not to initiate the rosiglitazone arm because of the reported potential cardiovascular risks associated with rosiglitazone.

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

Rosiglitazone and Valsartan

Primary outcome measure

To compare beta-cell function, as reflected by the first phase insulin secretion corrected for insulin sensitivity and/or the arginine-stimulated insulin secretion, both co-primary endpoints as measured during the eu-hyperglycemic clamp procedure, following 52 weeks of rosiglitazone, valsartan or rosiglitazone combined with valsartan in subjects with IFG (with and without a family history of DM2) and/or IGT.

Secondary outcome measures

To compare the effects of 52 weeks of rosiglitazone, valsartan or rosiglitazone combined with valsartan in subjects with IFG (with and without a family history of DM2) and/or IGT with respect to:

1. Fasting plasma glucose
2. Second phase insulin secretion in response to hyperglycemia during the hyperglycemic clamp test
3. All the above-mentioned beta-cell function parameters at 12 weeks after discontinuation of therapy to assess durability/disease modifying effects
4. The conversion from Normal Glucose Tolerance (NGT) to IGT or diabetes (as evaluated by an oral glucose tolerance test)
5. HbA1c, fasting blood glucose and lipid/lipoprotein concentrations

6. Insulin sensitivity assessed during the euglycemic clamp test
7. Safety and tolerability, including assessments of hypoglycemic events, blood pressure, and urinary albumin excretion rate

Overall study start date

01/10/2006

Completion date

01/01/2010

Eligibility

Key inclusion criteria

1. Male and female subjects (aged 35 to 70 years)
2. Impaired Fasting Glucose (IFG): fasting plasma glucose 6.1 or higher and less than 7.0 mmol/l, or fasting plasma glucose 5.6 or higher and less than 7.0 mmol/l and a family history of Diabetes Mellitus type two (DM2) (i.e. first and second degree [i.e. grandparents] relatives)
3. Impaired Glucose Tolerance (IGT): two hour plasma glucose during 75 g oral glucose tolerance test 7.8-11.1 mmol/l

Participant type(s)

Patient

Age group

Adult

Sex

Both

Target number of participants

144

Key exclusion criteria

Drug use:

1. Current use of Angiotensin-Converting Enzyme Inhibitors (ACE-I), Angiotensin Receptor Blockers (ARB) and/or Thiazolidinediones (TZDs) and inability to discontinue these drugs
2. Known hypersensitivity to any of the study drugs
3. Prior use of blood glucose lowering medications except during pregnancy
4. Use of systemic glucocorticoids or niacin

Cardiovascular co-morbidities:

1. Ejection fraction known to be less than 40% or congestive heart failure, or existing clinical Cardio-Vascular (CV) disease:
 - a. previous Myocardial Infarction [MI] or stroke
 - b. angina with either more than 50% stenosis in more than or equal to two major coronary arteries, or ST depression of more than or equal to 2 mm, or a positive nuclear test, or previous coronary angioplasty, stent or bypass
 - c. previous limb bypass or vessel angioplasty or angiographic evidence of more than 50% stenosis, or intermittent claudication with an ankle/arm pressure less than or equal to 0.8
2. Uncontrolled hypertension requiring ACE-I or ARB

Other Criteria:

1. History of diabetes (except gestational DM) or on anti-diabetic medication
2. Renal or Hepatic Disease:
 - a. renal artery stenosis
 - b. creatinine clearance less than 40 ml/min or serum creatinine 200 umol/l or higher
 - c. clinical proteinuria (one or above, positive proteinuria on dipstick or 300 mg and above albuminuria/day, in the absence of urine)
 - d. measured Alanine Transferase (ALT) 2.5 or more times the upper limit of normal
 - e. active liver disease including jaundice, chronic hepatitis, previous liver transplant
3. Major illness with life expectancy of less than five years or that may interfere with participation
4. Use of another experimental drug
5. Pregnant or unwilling to use reliable contraception (fertile women will have a pregnancy test prior to randomisation)
6. Major psychiatric disorder
7. Diseases and medications that affect glucose tolerance (e.g. pheochromocytoma, Cushing's syndrome, acromegaly, steroid-dependent asthma, protease inhibitors, anti-psychotics)
8. Unwillingness to be randomised or sign informed consent)
9. Known uncontrolled substance abuse
10. Inability to understand study information and/or communicate with clinic staff

Date of first enrolment

01/10/2006

Date of final enrolment

01/01/2010

Locations

Countries of recruitment

Netherlands

Study participating centre

VU University Medical Center

Amsterdam

Netherlands

1081 HV

Sponsor information

Organisation

VU University Medical Center (The Netherlands)

Sponsor details

Van der Boechorststraat 7

Amsterdam

Netherlands
1081 BT

Sponsor type

Hospital/treatment centre

ROR

<https://ror.org/00q6h8f30>

Funder(s)

Funder type

Industry

Funder Name

Novartis Pharma B.V. (The Netherlands)

Funder Name

GlaxoSmithKline (The Netherlands)

Alternative Name(s)

GlaxoSmithKline plc., GSK plc., GSK

Funding Body Type

Government organisation

Funding Body Subtype

For-profit companies (industry)

Location

United Kingdom

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?
Results article	further results	01/05/2012		Yes	No
Results article	results	01/09/2012		Yes	No
Results article	results	01/05/2013		Yes	No