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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	Recruitment status
28/09/2006	No longer recruiting
Registration date	**Overall study status**
28/09/2006	Completed
Last Edited	**Condition category**
08/07/2013	Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] 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

Contact name
Dr M Diamant

Contact details
VU University Medical Center
Department of Endocrinology
Diabetes Center
De Boelelaan 1117
P.O. Box 7057
Amsterdam
Netherlands
1081 HV
+31 (0)20 4440534
m.diamant@vumc.nl

Additional identifiers

Protocol serial number

N/A

Study information

Scientific Title

Acronym
PRESERVE TRIAL

Study objectives
Type two diabetes is cause 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 develope type two diabetes, including those with impaired fasting glucose and/or impaired glucose tolerance (with/without a familiy 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

Study type(s)
Treatment

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(s)
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.

Key secondary outcome(s))
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

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

Healthy volunteers allowed
No

Age group
Adult

Sex
All

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, Cushings 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)

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., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

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
Study website	Study website	11/11/2025	11/11/2025	No	Yes