Effect of adding vildagliptin to start of insulin treatment in patients with type 2 diabetes

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Is addition of a DPP4-inhibitor (vildagliptin) beneficial in type 2 diabetic patients, starting on once daily long-acting insulin in combination with 2 dd metformin. Primary end point is necessary dose of insulin to remain glycemic control....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON37974

Source
ToetsingOnline

Brief title
Vildagliptin and insulin in type 2 diabetes

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Novartis

Intervention

Keyword: insulin, type 2 diabetes, Vildagliptin

Outcome measures

Primary outcome

required insulin dose after 16 weeks of treatment.

Secondary outcome

- weight

- hypoglycemias

- glucose variability (measured by continuous glucose monitoring system)

- insulin and glucagon levels after mixed meal test

- HbA1c, fructosamine

- 24 hours measured blood pressure

- lipid profile

- markers of vascular function, inflammation and coagulation

- advanced glycation end products measured by skin autofluorescence

Study description

Background summary

Type 2 diabetes is characterized by progressive beta cells, causing deterioration of beta cell function. Due to this progressiev nature of the disease, at a certain point oral glucose lowering drugs in combination with diet cannot establish normoglycemia anymore. At this poit the patient should start insulin treatment. Usually once daily long-acting insulin is then started. Insulin treatment usually results in weight gain and increases the change for hypoglycemia.
A lot of research looks into the effect of oral glucose lowering drugs added to insulin on HbA1c, as a measure of glycemic regulation. Studies with DDP4-inhibitors showed, significant reduction of HbA1c , when added to insulin,

where the insulin regimen was kept the same. This was seen in combination with less hypoglycemias. But in daily clinical practice insulin regimens will be modified according to glycemic variation, and not HbA1c but insulin doses are the primary effect.
The mechanism of better glycemis control of combination of DPP4-inhibitors and insulin includes a glucose dependent insulin secretion (in contrast to for instance sulfonyl ureum derivates, which give a constant beta cel stimulation, unrelated to glucose) with the DPP4-inhibitors, as well as decreases in glucagon production (hyperglucagonemia is a problem in diabetes). Resulting in less endogeneous glucose production.
The primary effect of this study will be the necessary dose of insulin required. Secundary end points are parameters related to glucose regulation (continuous glucose measurement CGMS), insulin and glucagon levels after standardized mixed meal tests, vascular effects (24 hours blood pressure measurement, lipids), changes in advanced glycation end products (AGEs, measured by skin autofluorescence).

Study objective

Is addition of a DPP4-inhibitor (vildagliptin) beneficial in type 2 diabetic patients, starting on once daily long-acting insulin in combination with 2 dd metformin. Primary end point is necessary dose of insulin to remain glycemic control. Secundary end points are hypoglycemia, weight, glucose variability, parameters after mixed meal test and cardio-vascular parameters.

Study design

Patients with type 2 diabetes are randomized between insulin and metformin treatment with vildagliptin and insulin and metformin treatment with placebo.
The following parameters are measured at the begin and at the end of the study:
Primary parameter:
- required insulin dose
Secondary parameters:
- weight
- hypoglycemias
- glucose variability
- insulin and glucagon levels after mixed meal test
- HbA1c, fructosamine
- 24 hours measured blood pressure
- lipid profile
- markers of vascular function, inflammation and coagulation
- advanced glycation end products measured by skin autofluorescence

Intervention

Normal insulin treatment with fixed dose metformin, combined with vildagliptin

(intervention group) or placebo (control group).

Study burden and risks

The insulin treatment itself is the same as usual. But metformin is given as a fixed dose (2 dd 850 mg) and all other oral antihyperglycemic agents are discontinued in this study. Patients should attend the outpatient clinic more often (4 times). The only study so far combining insulin and vildagliptin showed a good tolerability and significant less hypo's in the patients taking vildagliptin. Based on this prior study we expect the risk for patients taking a combination of vildagliptin and insulin to be low. Furthermore in patients with deteriorating glycemic controol (hbA1c + > 1.0%) the study will be stopped.
The secondary parameters require a few more tests, which gives the extra burden, consisting of:
- the continuous glucose monitoring system (requires patients to have a small subcutenuous needle attached to a monitoring device for 72 hours), this device is also used in daily clinical practice to optimize glucose control
- 24 hours blood pressure measurement (requires the patient to wear a blood pressure band, measuring the blood pressure every 30 minutes for 24 hours), again this is frequently used in daily clinical practice
- AGE-reader (a device that illuminates the fore arm for a few seconds with ultraviolet light)
- mixd meal test (continuous blood sampling during 3.5 uur in the outpatient clinic)

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Type 2 diabetes
Failure on oral medication and start of insulin treatment with once daily long-acting insulin (glargine)
HbA1c 7-9%
BMI 25-35
Age 25-75

Exclusion criteria

-Pregnant women or women in the fertile period of life without adequate birth-control
-Type I DM, or secondary form of DM (eg pancreatic injury, prednisone induced)
- Acute metabolic complications (severe hypoglycaemia, hospital-admission for uncontrolled hyperglycemia) during the last 6 months
- Severe cardiac (LVEF < 30%) or a history of or current hepatic, or renal impairment (creatinine clearance <50 ml/min)

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-12-2009
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Galvus
Generic name:	Vildagliptin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	29-09-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	11-11-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-07-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-01-2011
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-02-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-03-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-02-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-04-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 29400
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2009-010967-18-NL
CCMO	NL26046.041.09
OMON	NL-OMON29400