Effects of GLP1 agonist liraglutide in patients with antipsychotic-drugs-associated diabetes mellitus

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1. To assess the efficacy of liraglutide in patients with schizophrenia and diabetes ona. Glycaemic controlb. Body weightc. Cardiovascular risk factors (blood pressure, lipids)2. To assess the safety of liraglutide in these patients3. To assess the...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON40321

Source
ToetsingOnline

Brief title
GRADUATE

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes Mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Interne geneeskunde
Source(s) of monetary or material Support: Novo Nordisk,NovoNordisk

Intervention

Keyword: Antipsychotic drugs, Diabetes mellitus, GLP-1, Liraglutide

Outcome measures

Primary outcome

* Change in HbA1c (end of trial * baseline value)

Secondary outcome

* Change in BMI and intra-abdominal fat mass (CT scan)

* Change in cardiovascular risk factors

o Lipid profile

o Blood pressure

* Safety

o Hypoglycaemia

o Adverse events

* Compliance

* Patient-reported outcomes

o Diabetes-related (PAID, EQ5D, SF12, DTSQ)

o Psychiatry-related (CAIG, PANSS)

* Continuous glucose monitoring

Study description

Background summary

Patients treated with antipsychotic drugs have an increased incidence of diabetes and the metabolic syndrome, attributable to a large degree to the use of anti-psychotic drugs. Anti-psychotic drugs are strongly obesiogenic and diabetogenic. Diabetes and the metabolic syndrome are held responsible for the

increased incidence of cardiovascular diseases in treated patients with schizophrenia and help to explain their decreased life expectancy. Diabetes is difficult to treat in these patients, also because of limited compliance. Liraglutide as a GLP1-agonist holds promise as a new therapeutic avenue, combining glycaemic efficacy and weight-losing properties with low risk of side effects and easy therapeutic scheme.

Study objective

1. To assess the efficacy of liraglutide in patients with schizophrenia and diabetes on
a. Glycaemic control
b. Body weight
c. Cardiovascular risk factors (blood pressure, lipids)
2. To assess the safety of liraglutide in these patients
3. To assess the compliance with liraglutide use in these patients
4. To asses patient reported outcomes including general ones and schizophrenia-related ones
5. To explore the effect of liraglutide on the intra-abdominal fat mass as assessed by one -slice CT-scan

Study design

The study is designed as a six-month, randomised (1:1), double-blind, parallel-armed, placebo-controlled clinical trial comparing liraglutide versus liraglutide-placebo on top of usual metformin therapy.

Intervention

This is a randomised placebo-controlled parallel arm intervention study in metformin-treated patients with schizophrenia and anti-psychotic drugs-related diabetes mellitus. During a 6-month trial, patients will receive either liragutide 1.8 mg sc (rapidly uptitrated) or placebo sc. There are 25 patients in each treatment group.

Study burden and risks

Particpation in this trial requires 5 visits to the hospital, eacht takning one hour.
Blood sampling will be done 4 times.
Liraglutide is associated with an increased risk of abdominal complaints (like nausea; moderate risk)
Subcutaneous injedtion can lead to lcocal irritation of small bleeding (moderate risk)

Contacts

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Selecteer

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Severe mental disorder (schizophrenia and schizophrenia-related; these disorders are defined with one of the following DSM-codes: 295.10, 295.20, 295.30, 295.40, 295.60, 295.70, 295.90, 297.1, 297.3, 298.8, 298.9)
* Informed consent obtained before any trial related activities
* Males or females aged 18 years or older
* Diabetes mellitus developed while on anti-psychotic drugs, Diabetes Mellitus for at least six months
* Use of metformin for the treatment of diabetes for at least three months
* HbA1c >7.0% - * 10.0 mmol/l (53 * 69 mmol/mol)
* BMI 30 * 45 kg/m2
* Regarded capable to understand and follow the protocol

Exclusion criteria

Any type of diabetes present prior to the use of anti-psychotic drugs (including type 1 diabetes)
* Use of glucose-lowering medication other than metformin, current use of within 3 months prior to start of the study
* Any cardiovascular event in the last 6 months
* Reduced cardiac function (LVEF < 30%)
* Any evidence of active retinopathy
* Uncontrolled hypertension (systolic pressure > 180 mm Hg and/or diastolic pressure > 100 mm Hg
* Compromised renal function (MDRD < 60 ml/min)
* Liver function abnormalities (ALT and/or AST > 3 times the upper limit of normal)
* History of chronic pancreatitis or previous acute pancreatitis
* Known or suspected hypersensitivity to trial product(s) or related product(s)
* Female of child-bearing potential who is pregnant, breast-feeding or intending to become pregnant or is not using adequate contraceptive methods
* Participation in another trial or receipt of any investigational medicinal product within 90 days prior to screening
* Subjects who are considered incapable for inclusion by their physicians
* Subjects who are considered inadequate for liraglutide administration themselves and lack network of support
* Subjects who are actively suicidal
* Recurrent use of corticosteroids
* Personal or family history of medullary thyroid carcinoma and patients with multiple endocrine neoplasia type 2 (MEN2)
* Known or suspected abuse of alcohol or narcotics during the trial

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	50
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Victoza
Generic name:	Liraglutide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	10-09-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	06-02-2015
Application type:	First submission
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2013-005395-18-NL
CCMO	NL47408.041.13