In Vivo Imaging of Neuroinflammation in Simvastatin-Treated Schizophrenic Patients

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The primary objective of this study is to determine if the binding of [11C]PK11195, as a measure of neuroinflammation, in schizophrenic patients is decreased after simvastatin treatment.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Schizophrenia and other psychotic disorders
Study type	Observational invasive

Summary

ID

NL-OMON45184

Source
ToetsingOnline

Brief title
Neuroinflammation in SIM-treated SCZ patients

Condition

- Schizophrenia and other psychotic disorders

Synonym
schizophrenia

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: ZonMW TOP grant

Intervention

Keyword: Neuroinflammation, Positron Emission Tomography, Schizophrenia, Simvastatin

Outcome measures

Primary outcome

The main study parameter is the [11C]PK11195 binding potential in the brain.

Secondary outcome

n/a

Study description

Background summary

Schizophrenia is a severe mental disorder placing significant burden on global health. Although antipsychotic medication can improve the clinical symptoms, schizophrenia is still causing considerable morbidity and mortality. The pathogenesis of schizophrenia is still far from elucidated which hampers the development of novel pharmacological therapies. Different lines of evidence now suggest that low grade neuroinflammation is involved in the pathogenesis of schizophrenia. Anti-inflammatory drugs can thus be viewed as potential candidates for new augmentation therapies. A statin could provide anti-inflammatory treatment and may have particular potential as adjuvant therapy in patients with recent-onset schizophrenia. A treatment trial with simvastatin was recently initiated (core trial, METc Utrecht 13/249, clinicaltrials.gov NCT01999309). In this study we will examine the effect of simvastatin on neuroinflammation, using [11C]PK11195 positron emission tomography (PET), in a subgroup of the patients in the core trail.

Study objective

The primary objective of this study is to determine if the binding of [11C]PK11195, as a measure of neuroinflammation, in schizophrenic patients is decreased after simvastatin treatment.

Study design

This PET study is an observational, multi-center study. The subjects will undergo a PET scan with the TSPO ligand [11C]PK11195, which is a marker for

microglia activation in neuroinflammation.

Study burden and risks

The subjects in this study will undergo a [11C]PK11195 PET scan during which 160 ml of blood is taken for radioactivity and radiometabolites measurements. Female subjects have to undergo a pregnancy test prior to the PET scan. Healthy controls will undergo the PET scans once. The schizophrenic patients will undergo two PET scan, one before and after 12 months of simvastatin treatment. Healthy controls will additionally undergo an MRI scan.
For the PET study, the only adverse event can be a bruise as a result of the arterial catheter. In addition, according to the International Commission on Radiological Protection (ICRP62) the radiation level of 2.0 mSv (for healthy control) or 4.0 mSv (for schizophrenic patients) is within category IIb (1-10 mSv, minor to moderate risk). The subjects will not directly benefit from the study, but will help to evaluate if neuroinflammation is present schizophrenia and if this is reduced by simvastatin treatment. This can lead to additional studies on the role of neuroinflammation in schizophrenia and to improved or new treatment strategies.

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

Control subjects
> Age between 18 and 50 years.;Schizophrenic patients
Fulfilling the inclusion of the core study, which are:
> Age between 18 and 50 years;
> A DSM-IV-R diagnosis of: 295.x (schizophrenia, schizophreniform disorder, or schizoaffective disorder) or 298.9 (psychosis NOS);
> Onset of first psychosis no longer than 3 years ago;
> Female patients of childbearing potential need to utilize a proper method of contraception (the pill, vaginal ring, hormonal patch, intrauterine device, cervical cape, condom, contraceptive injection, diaphragm) in case of sexual intercourse during the study.

Exclusion criteria

Control subjects
> Women who are pregnant;
> Women who intend to get pregnant during the study;
> Use or having used psychotropic medication in the past six months;
> Alcohol or substance abuse in the past 3 months;
> Taking any medication, except oral contraceptives;
> Evident somatic/psychiatric co-morbidity;
> First-degree relatives with (a history of) schizophrenia or schizophrenia spectrum disorders;
> Participation in a scientific research study during the past year involving radiation;
> Presence of materials in the body that can be magnetized and cannot be removed.;Schizophrenic patients
Fulfilling the exclusion of the core study, which are:
> Fulfilment of criteria of statin prescription; according to the Dutch Heart Foundation (Hartstichting), statin treatment is indicated when the total cholesterol level is >8 mmol/l (www.hartstichting.nl);
> Presence of any of the contra-indications or warnings for the use of simvastatin as reported in the SPC;
> Chronic use of glucocorticosteroids (temporary use is permitted, if stopped at least 1 month before start of treatment trial);
> Chronic use of non-steroidal anti-inflammatory drugs (temporary use is permitted, if stopped at least 1 month before start of treatment trial);
> Current use of statins or other lipid-lowering drugs;

> Pregnancy or breast-feeding;
> Active liver, kidney or muscle disease as defined by alanine aminotransferase (ALAT), creatinine or creatine kinase (CK) levels more than two times the upper boundary of normal levels;
> Use of comedication that either inhibits or induces the live enzyme CYP3A4 which is responsible for the degradation of simvastatin. Inhibitors of CYP3A4 include itraconazole, ketoconazole, posaconazole, fluconazole, erythromycin, clarithromycin, telithromycin, HIV protease inhibitors, nefazodone, telaprevir, boceprevir, imatinib, ticagrelor, voriconazole; inducers of CYP3A4 include carbamazepine, efavirenz, nevirapin, etravirin (can be washed out before start of trial);
> Use of comedication that may increase the risk for myalgia, rhabdomyolysis and myopathy, including colchicine, bosentan, fenobarbital, fenytoin, hypericum, rifabutin, rifampicin, fibrates (e.g. gemfibrozil), fusidic acid, carbamazepine (can be washed out before start of trial)
> Use of non-steroidal anti-inflammatory drugs (NSAIDs) one week before the PET scan;
> Alcohol or substance abuse in the past 3 months;
> Participation in a scientific research study during the past year involving radiation;
> Presence of materials in the body that can be magnetized and cannot be removed.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-03-2017
Enrollment:	75
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[11C]PK11195
Generic name:	[11C]PK11195

Ethics review

Approved WMO Date:	20-04-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-06-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-05-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-08-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-02-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2015-001599-23-NL
CCMO	NL53149.042.15