Validation of the novel PET tracer [18F]PK209 in healthy volunteers: Dosimetry, test-retest, and specific binding to the NMDA receptor

Published: 06-08-2014
Last updated: 21-04-2024

The objective of this project is to assess the applicability of [18F]PK209 for in vivo imaging of the NMDA receptor.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON40871

Source
ToetsingOnline

Brief title
[18F]PK209 first in human PET

Condition

- Other condition
- Neurological disorders NEC
- Schizophrenia and other psychotic disorders

Synonym
there is no disease

Health condition

onderzoek heeft in de toekomst betrekking op bovenstaande aandoeningen, maar wordt uitgevoerd bij gezonde controles

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: CTMM

Intervention

Keyword: dosimetry, NMDA receptor, positron emission tomography

Outcome measures

Primary outcome

1) To assess the whole body biodistribution and dosimetry of [18F]PK209

2) To examine the regional brain uptake, metabolites, and test-retest

variability of [18F]PK209

3) To examine the specific binding potential of [18F]PK209 in the brain before

and after ketamine displacement

Secondary outcome

not applicable

Study description

Background summary

NMDA receptor (NMDA-R) dysfunction is present in a wide range of neurological and psychiatric diseases. In the last decade, a major effort in NMDA-R drug development has focussed on pharmacological modulation of the PCP binding site of the NMDA-R binding site as treatment for a wide range of neurological and psychiatric CNS pathologies, including stroke, head trauma, depression, cognitive disorders and dementias.

In vivo quantification of the NMDA-R using positron emission tomography (PET) has long been an elusive goal in nuclear medical imaging. A widely implementable, well validated radiotracer would be a highly valuable tool for

assessing both NMDA-R availability and its etiology in neurodegenerative and neuropsychiatric diseases. Importantly, links between academia and industry can be strengthened; A novel PET radiotracer that can target the NMDA receptor would allow assessment of the binding of CNS drugs, which will be of high interest for the development of novel pharmaceuticals.

Recently, a new class of PCP ligands were developed at the VUmc, such as [11C]GMOM and [18F]PK209, which offer the opportunity investigate the NMDA-R complex in vivo. Radiochemists at the VUmc have succeeded in synthesizing [18F]PK209 in high yield. The tracer was evaluated as an NMDA-R selective PET radioligand in mice and rats, and passed key tracer development decision points in a multitude of experiments.

Study objective

The objective of this project is to assess the applicability of [18F]PK209 for in vivo imaging of the NMDA receptor.

Study design

The study consists of three sub studies with three groups of healthy subjects according to the three objectives. 14 men and women are allowed to participate in this study with the age range from 18 to 70 years old. In the first group (N=4) the dosimetry of [18F]PK209 will be assessed. In the second group (N=4) the brain uptake of [18F]PK209 and variability will be assessed, with 2 PET scans. In the third group (N=6) the specific binding of [18F]PK209 to the NMDA receptor will be investigated, by comparing the PET scans of the brain before and after the administration of 0,5 mg/kg S-ketamine.

Study burden and risks

Risks associated with participation in this study are related to radiation exposure, placement of intra-venous and arterial catheters, blood sampling, discomfort during scanning, and (in cohort 3 only) adverse events in response to ketamine administration.

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

1. Signed informed consent prior to any study-mandated procedure.
2. Healthy male and female subjects, 18 to 70 years of age (inclusive). Healthy status is defined by absence of evidence of any active or chronic disease following a physical examination by a trained physician (assistant), and no clinically significant abnormal results in haematology, blood chemistry, and urinalysis.
3. Body mass index (BMI) between 18 and 34 kg/m2 (inclusive), and with a minimum weight of 50 kg.
4. Able to communicate well with the investigator in the Dutch language and able to comply with the study restrictions.
5. Able to lie comfortably in the PET scanner for a period of two hours.

Exclusion criteria

1. Any known factor, condition, or disease that might interfere with study compliance, study conduct or interpretation of the results such as drug or alcohol dependence or psychiatric disease.
2. Positive test for drugs of abuse at screening or pre-PET.
3. Intake of an investigational medicinal product within 30 days prior to the start of this study.
4. Loss or donation of blood over 500 mL within three months (males) or four months

(females) prior to screening.
5. Any condition that may interfere with MRI scanning, e.g. metal objects in or around the body or claustrophobia
6. Pregnant (as tested within 24 hours of the PET scan) or breastfeeding.
7. Inclusion in a research protocol in the past 3 years involving ionizing radiation, which would result in exceeding the ICRP category IIb limit of 10 mSv in addition to natural background radiation.
8. Unacceptable non-pharmacological substances or concomitant medications at baseline. Especially drugs that extend the QT-interval, or (only for cohort 3) drugs that may interact with ketamine (inhibitors of CYP2B6, CYP2C9, CYP3A4) or any other drugs known or likely to affect with study assessments.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2014
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]PK209
Generic name:	[18F]PK209

Ethics review

Approved WMO

Date:	06-08-2014

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-10-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	EUCTR2014-001735-36-NL
CCMO	NL49180.029.14