Test-retest of the P-gp PET tracer [11C]laniquidar in healthy volunteers.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON27121

Source
NTR

Health condition

healthy volunteers

Sponsors and support

Primary sponsor: VU University Medical Center
Source(s) of monetary or material Support: European Community’s Seventh Framework Programme grant (EURIPIDES)

Intervention

Outcome measures

Primary outcome

To determine plasma and brain kinetics, and radiometabolites of [11C[laniquidar in human.

Secondary outcome

1. To develop a tracer kinetic model for [11C]laniquidar in human;

2. To determine intra-subject variation of [11C]laiquidar in human.

Study description

Background summary

Resistance to current drug therapy is an issue for approximately 30% of all people who develop epilepsy. Consequently, there is a pressing need to develop new and more effective treatments.
P-glycoprotein (P-gp) seems to be involved in drug resistance. P-gp is an efflux transporter (member of the multi-drug resistance (MDR) family), which is located at the blood-brain barrier (BBB) and transports substrates (including multiple CNS drugs) from brain to blood and cerebrospinal fluid. Overexpression of P-gp is thought to be an important mechanism of pharmacoresistance in epilepsy. Various invasive techniques used in animal studies of epilepsy showed upregulation of P-gp. At present upregulation of P-gp in refractory patients can only be confirmed by examining brain tissue post-mortem or after surgical removal. Therefore availability of non-invasive imaging methods that would allow for an assessment of distribution and function of P-gp in the brain is of vital importance.

At present only (R)-[11C]verapamil is available for assessing P-gp function using PET. Verapamil is a substrate of P-gp and therefore cerebral concentration is low. In case of overexpression of P-gp, it is likely that the signal will be even further reduced, but this is difficult to assess due to the low signal to noise ratio. Consequently, (R)-[11C]verapamil is not an ideal ligand for assessing P-gp (over)expression. Therefore novel PET probes, designed to specifically measure P-gp expression, need to be developed.

Laniquidar is an antagonist of P-gp and therefore it should bind in a dose dependent manner. Recently, this compound was labelled with carbon-11, making it a potential tool for measuring P-gp expression. Initial results of brain uptake of [11C]laniquidar in rats were inconclusive. The rat biodistribution studies in peripheral organs showed the highest uptake in the spleen, heart, kidney and lung. This might be due to the formation of labelled metabolites.

Nevertheless, as the metabolite profile of (R)-[11C]verapamil is completely different between humans and rats, only direct studies in humans can be used to determine whether [11C]laniquidar is a potent tracer to assess P-gp expression in vivo. Furthermore, paired [11C]laniquidar scans are needed to determine intra-subject variation of [11C]laniquidar plasma and brain kinetics of [11C]laniquidar.
Each [11C]laniquidar scan is acquired following an intravenous injection of 370 MBq. The radiation dose associated with 370 MBq of [11C]laniquidar is 2 ± 0.4 milliSievert (mean ± SD). These data have been obtained from our recently performed dosimetry and biodistribution study in healthy subjects.

Study objective

[11C]laniquidar has favourable brain and plasma kinetics, and also a small intra-subject variation in humans.

Study design

One timepoint measurement (two scans on one day).

Intervention

370MBq [11C]laniquidar was injected iv., simultaneously a 60-minute dynamic emission scan will be started. Furthermore, blood samples will be taken.

Contacts

Public
P.O.Box 7057
E.A.M. Froklage
Amsterdam 1007 MB
The Netherlands
+31 (0)20 4445214
Scientific
P.O.Box 7057
E.A.M. Froklage
Amsterdam 1007 MB
The Netherlands
+31 (0)20 4445214

Eligibility criteria

Inclusion criteria

1. Age between 18-65 years;

2. Good physical health;

3. Weight > 50kg;

4. Not pregnant;

5. Written informed consent.

Exclusion criteria

1. Any significant abnormality of any clinical laboratory test;

2. Use of investigational medication in the previous 30 days;

3. Major psychiatric or neurologic disorder, or history of coagulation problems.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-06-2011
Enrollment:	12
Type:	Anticipated

Ethics review

Positive opinion

Date:	22-06-2011
Application type:	First submission

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
NTR-new	NL2819
NTR-old	NTR2960
Other	METC VUmc : 2011-75
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A