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

Gepubliceerd: 22-06-2011 Laatst bijgewerkt: 18-08-2022

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

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON27121

Bron
NTR

Aandoening

healthy volunteers

Ondersteuning

Primaire sponsor: VU University Medical Center
Overige ondersteuning: European Community’s Seventh Framework Programme grant (EURIPIDES)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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

Onderzoeksopzet

One timepoint measurement (two scans on one day).

Onderzoeksproduct en/of interventie

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

Contactpersonen

Publiek

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

Wetenschappelijk

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

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age between 18-65 years;

2. Good physical health;

3. Weight > 50kg;

4. Not pregnant;

5. Written informed consent.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	22-06-2011
Aantal proefpersonen:	12
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	22-06-2011
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2819
NTR-old	NTR2960
Ander register	METC VUmc : 2011-75
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A