PKAN phase-II

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Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24533

Bron
NTR

Verkorte titel
4’PPT for PKAN

Aandoening

Pantothenate Kinase-Associated Neurodegeneration (PKAN)

Ondersteuning

Primaire sponsor: Department of Biomed. Sciences of Cells & Systems. Section: Molecular Cell Biology. University Medical Center Groningen This is an investigator-initiated study
Overige ondersteuning: 1. ZonMw
2. Hersenstichting
3. Stichting Lepelaar will financially contribute to the study if needed.

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1) to obtain in vivo pharmacokinetic data of 4’-PPT (the study product) measured in plasma of PKAN patients;

2) to obtain pharmacodynamic data of the biomarker COASY in circulating lymphocytes of PKAN patients, when 4’-PPT is provided daily at 3 subsequent increasing doses (7,5 mg/m2, 15 mg/m2 and 30 mg/m2) for a month each and when 4’-PPT has been orally provided over a period of 19 months on a fixed dose, based on the biomarker measurements obtained from the dose-escalation phase.

Toelichting onderzoek

Achtergrond van het onderzoek

Background- Pantothenate kinase-associated neurodegeneration (PKAN) is an ultra-rare neurodegenerative disease affecting children and adults. Patients suffer from progressive generalized dystonia, parkinsonism and brain iron accumulation. No treatment exists for this disease. PKAN patients lack an enzyme required for biosynthesis of coenzyme A, an essential co-factor for numerous cellular metabolic reactions.
Compelling preclinical evidence shows that 4’-phosphopathetheine (4’-PPT), a downstream metabolic product of the enzyme lacking in PKAN, completely rescues the disease phenotype in PKAN animal and human cell models. Preclinical studies also identified a biomarker for a coenzyme A biosynthetic enzyme downstream from the defective enzyme in PKAN: “COASY”.

Purpose- Our study aims to collect for the first-time in vivo pharmacokinetic information of 4’-PPT, when orally administered, in PKAN patients. In addition, we will collect COASY biomarker information in relation to 4-PPT plasma concentrations. With this information, more rational dosages and dosing schedules can be designed for future 4-PPT treatment.

Methods- We perform a within-subject dose-escalation study, investigating 3 subsequent increasing doses during 5 months followed by an open label extension study of 19 months (on a fixed dose). Simultaneously we will collect information regarding safety and tolerability.

Study population- Children and adults with genetically confirmed PKAN disease. We included 10 PKAN patients in this study from the Netherlands and Belgium.

Doel van het onderzoek

We hypothesize this study will generate useful pharmacokinetic information of 4’-PPT, and we expect it will be safe and well tolerated.

Onderzoeksopzet

Patients will be visited at home 10 times during the first 5 months (M0-M4) of the dose-escalation phase. During the extension study, 1 visit after 1 year will occur and 1 visit at the end of the trial. Blood collection will occur at 10 home visits for 4’-PPT and COASY, plus routine safety laboratory tests. A standard video-recording will be taken at 6 of the visits to monitor the neurological status of the patient, and regular telephone contact will occur

between the home visits as needed.

Onderzoeksproduct en/of interventie

All patients will be given 4’-PPT. Patients will be assigned a daily dose of 4’- PPT, that will be provided orally in 3 subsequent increasing doses during 5 months followed by an open label extension study of 19 months (on a fixed dose).

Contactpersonen

Publiek

UMCG
Marleen Bracke

0637301204

Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Have a diagnosis of PKAN confirmed by genetic testing showing two pathogenic mutations, OR one confirmed mutation and typical clinical and imaging features of the disease.
2. Aged >12 months at the time of screening.
3. Be able to take the study product by oral route or via gastrostomy tube.
4. Informed consent is provided by the patient and/or parents and/or legal representative
5. Be resident in The Netherlands or Belgium for the duration of the trial.
6. Be in the possession of a Dutch or Belgium health insurance.

Belangrijkste redenen om niet deel te kunnen nemen

(Exclusiecriteria)

For inclusion in this trial,
1. Subjects must NOT have been exposed to a putative PANK2 ‘bypass’ therapeutic agent in the 30 days prior to screening.
2. Subjects must NOT be concurrently enrolled in another interventional clinical trial.
3. Subjects must NOT have concurrent medical or other conditions that in the opinion of the investigators are expected to preclude completion of study procedures or confound the assessment of clinical and laboratory measures of safety.
4. Subjects who do NOT understand Dutch.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	04-09-2021
Aantal proefpersonen:	10
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Ja

Ethische beoordeling

Positief advies

Datum:	02-11-2021
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 55013
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9855
CCMO	NL73850.000.20
OMON	NL-OMON55013

Resultaten