PKAN phase-II

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24533

Source
NTR

Brief title
4’PPT for PKAN

Health condition

Pantothenate Kinase-Associated Neurodegeneration (PKAN)

Sponsors and support

Primary sponsor: Department of Biomed. Sciences of Cells & Systems. Section: Molecular Cell Biology. University Medical Center Groningen This is an investigator-initiated study
Source(s) of monetary or material Support: 1. ZonMw
2. Hersenstichting
3. Stichting Lepelaar will financially contribute to the study if needed.

Intervention

Outcome measures

Primary outcome

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.

Secondary outcome

1) To assess safety and tolerability of the used doses of 4’-PPT in PKAN patients when 4’-PPT is orally provided;
2) Objective neurological examination (video) .

Study description

Background summary

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’-phosphopatheteine (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.

Study objective

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

Study design

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.

Intervention

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).

Contacts

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Eligibility criteria

Inclusion criteria

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.

Exclusion criteria

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.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-09-2021
Enrollment:	10
Type:	Actual

IPD sharing statement

Plan to share IPD: Yes

Ethics review

Positive opinion

Date:	02-11-2021
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 55013
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

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

Study results