Pharmacokinetic - pharmacodynamic study of amifampridine modified release in LEMS patients

Published: 14-08-2024
Last updated: 27-12-2024

The aim of this study is to investigate the pharmacokinetics of the extended release formulation of amifampridine. Secondary objective of the study is to develop a PKPD model of amifampridine in LEMS.

Ethical review	Approved WMO
Status	Pending
Health condition type	Neuromuscular disorders
Study type	Observational invasive

Summary

ID

NL-OMON56948

Source
ToetsingOnline

Brief title
PKPD of amifampridine MR in LEMS patients

Condition

- Neuromuscular disorders

Synonym
Lambert-Eaton Myasthenic Syndrome, LEMS

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Subsidie vanuit ministerie van VWS aan het Nationaal Farmaceutisch KennisCentrum (NFKC)

Intervention

Keyword: Amifampridine, LEMS, Modified release, PKPD

Outcome measures

Primary outcome

Pharmacokinetic parameters: Tmax, Cmax, AUC, VD, Ctrough,SS.

Secondary outcome

Pharmacodynamic endpoints: 3TUG scores, subject global impression (SGI) and

CMAP amplitude. The occurrence of side effects will also be assessed.

Study description

Background summary

Lambert-Eaton myasthenic syndrome (LEMS) is a very rare antibody-mediated autoimmune disease of the neuromuscular junction. LEMS is characterized by muscle fatigability with weakness in the limb girdle region as most important complaint. Therapy can be divided in symptomatic treatment and immunosuppressive treatment. Symptomatic treatment with amifampridine is the only therapy currently authorized for use in LEMS patients. In the Netherlands the first choice drug is amifampridine base in an extended release formulation, instead of the currently authorized amifampridine phosphate in an immediate release formulation. Although amifampridine base has not received formal authorisation, its use is condoned by regulating authorities based on the extensive (>40 year) experience with this drug, its lower costs and possibly better safety profile due to its extended release properties. However, the extended release properties of the formulation have been shown solely in in vitro dissolution experiments, no in vivo pharmacokinetic parameters have been collected.

Study objective

The aim of this study is to investigate the pharmacokinetics of the extended release formulation of amifampridine. Secondary objective of the study is to develop a PKPD model of amifampridine in LEMS.

Study design

A multiple dose open label study.

Study burden and risks

There is extensive experience with the use of amifampridine in patients with LEMS and the dose used in this study is based on the patients clinical response and side effects. Therefore the risk of serious (unexpected) side effects is minimal.

There is no medicinal product started in this study. The intervention entails extra measurements. Additional blood is collected and some pharmacodynamic endpoints are measured more frequent than in common clinical practice, the risk of these additional measurements is minimal. Additional risk may be the delay of the first daily dose of amifampridine because patients will travel to the research center withholding their first daily dose. The risk might be a minimal increase in symptoms of LEMS. A long travel time will increase this risk and an overnight stay near the research center will be offered to reduce this risk.

Benefits are more insight in the pharmacokinetics of amifampridine modified release and with this insight more optimal dosing regimes can be prescribed.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2300RC
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2300RC
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Age >18 years
2. Clinical diagnosis of LEMS
3. Presence of Voltage Gated Calcium Channel Antibodies (VGCC antibodies)
4. Current use of amifampridine modified release
5. Receiving a stable dose of amifampridine modified release

Exclusion criteria

1. The patient is unable to fill out the study questionnaires or be interviewed in Dutch or English, or is unable to undergo the tests needed for the study, or is unable to give informed consent for participation in the study.
2. The investigator can exclude patients for this trial which are deemed not suitable for any reason.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2024
Enrollment:	18
Type:	Anticipated

Ethics review

Approved WMO Date:	14-08-2024
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

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
CCMO	NL85775.058.24