HD-MED: Aiming to personalize drug treatment in Huntington’s Disease

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Primary objective: To classify the effect of the pharmacogenetic profile of CYP2C19 and CYP2D6 in HD gene expansion carriers on negative medication effects of HD-related medication with an actionable drug-gene interaction in the...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Movement disorders (incl parkinsonism)
Study type	Observational non invasive

Summary

ID

NL-OMON23607

Source
NTR

Brief title
HD-MED

Condition

- Movement disorders (incl parkinsonism)

Synonym
Pharmacogenetics, pharmacogenomics, drug type, medication use, medication efficacy, pharmacovigilance, Huntington’s Disease, rare disorder, protocol, biobank.

Health condition

Huntington's Disease

Research involving
Human

Sponsors and support

Primary sponsor: Leiden University Medical Center (investigator-initiated)
Source(s) of monetary or material Support: Investigator-initiated (LUMC), no conflicts of interest.

Intervention

Outcome measures

Primary outcome
Percentage per study protocol defined negative medication effects in HD gene expansion carriers with a CYP2C19 or CYP2D6 predicted poor and ultra-rapid metabolizer phenotype versus those with a predicted intermediate and normal metabolizer phenotype.

Secondary outcome
o Overview of medication use by HD gene expansion carriers in one year.

o Number of prescription drug discrepancies between the official pharmacy medication verification scheme and the patient-reported medication diary for the HD-MED follow-up period.

Exploratory outcome:

o Genetic variants associated with extra-ordinary side effect profiles or lack of medication response.

Study description

Background summary
Huntington's disease (HD) is a hereditary, neurodegenerative disorder characterized by motor, cognitive and psychiatric symptoms. Currently, HD can only be managed symptomatically, including a large variety in prescribed drugs. Many HD patients experience negative medication effects (e.g, side-effects or non-response). Pharmacogenetic (PGx)

studies show how individual genetic differences affect medication efficacy and toxicity, and holds the potential to explain and resolve these negative medication effects. This study aims to explore PGx interactions in HD to better guide the long-term pharmacological management of HD in a more personalized manner by reducing negative medication effects.

Study objective

Primary objective:

To classify the effect of the pharmacogenetic profile of CYP2C19 and CYP2D6 in HD gene expansion carriers on negative medication effects of HD-related medication with an actionable drug-gene interaction in the corresponding CYP genes. Negative medication effects are classified as non-response or side effects of the prescribed drug, which lead to definite prescription changes in that drug. Definite prescription changes are classified as; discontinuation of the drug, switching to another type of drug or adding another drug to treat the same symptom.

Secondary objectives:

o To assess and categorize current detailed medication use in HD gene expansion carriers.

o To determine the eligibility of a one-year medication diary compared to pharmacy medication history surveys in HD patients.

Explorative objectives:

o To explore the effect of the pharmacogenetic profile of CYP2C19 and CYP2D6 in HD gene expansion carriers who use HD-related medication and who either use a relatively low or a

relatively high drug dose with regard to the symptom the drug is prescribed for.

o To explore associations between genetic variants and extra-ordinary side effect profiles or lack of medication response in HD gene expansion carriers.

Study design

Inclusion period: 2.5 years Follow-up period: 1 year

Contacts

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Eligibility criteria

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

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria: - A capacitated individual, aged ≥ 18 years. - Genetically confirmed CAG-repeat expansion of ≥ 36 in the HTT gene. - Either about to start with prescribed medication related to HD or already using one or more HD related drugs. HD-related drugs are drugs considered to treat symptoms that either are related to manifest HD or are prescribed in pre-motor manifest or prodromal HD stage for symptoms that may be attributed to HD. - Sufficient knowledge of the Dutch language to understand the subject information letter and sign the informed consent form.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study: - Any medical condition, in the view of the investigator, which might endanger subject’s safety and/or satisfactory participation in the study.

Study design

Design

Study phase:	N/A
Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-01-2020
Enrollment:	391
Type:	Actual

IPD sharing statement

Plan to share IPD: No

Ethics review

Approved WMO

Date:	23-12-2019
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

ID: 55123
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL8251
Other	Medical Ethical Committee LDD (Leiden - Den Haag - Delft) : METC058
CCMO	NL70391.058.19
OMON	NL-OMON55123

Study results