Clonazepam in ARID1B Evaluation (CARE study)

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON29120

Source
NTR

Brief title
CHDR1939

Health condition

ARID1B

Sponsors and support

Primary sponsor: CHDR
Source(s) of monetary or material Support: CHDR

Intervention

Outcome measures

Primary outcome

Pharmacokinetic endpoints
Part A: serum and saliva. Part B: saliva only.
• The maximum serum concentration, Cmax
• The time to reach maximum serum concentration, tmax
• The terminal disposition rate constant (λz) with the respective half-life, t½

• The area under the serum concentration-time curve from zero to infinity, AUC0-inf
• The area under the serum concentration-time curve from zero to t of the last measured concentration above the limit of quantification, AUC0-last
• Clearance, Cl
• Volume of distribution, Vz

Trial@home endpoints
• Physical activity
• Sleep (duration, %light sleep, amount of times woken up)
• Heart rate
• Daily symptom scores
• Tapping frequency, adaptive tracking, animal fluency (twice-weekly)

Pharmacodynamic endpoints
• NeuroCart
o Adaptive Tracking
o Animal fluency test
o Body Sway
o Saccadic Eye Movements
o Smooth Pursuit Eye Movements
o Tapping frequency
• Questionnaires
o ABC questionnaire (parents, teacher)
o Clinician's Global Impression of improvement (CGI-I)

Tolerability / safety endpoints
• Adverse events
• Vital signs measurements
• General physical examination findings

Secondary outcome

N.A.

Study description

Background summary

Clonazepam is a registered and safe drug which is being used for the treatment of epilepsy. Preclinical experiments show that clonazepam rescues some of the preclinical phenotypes in ARID1B +/- mice. There is currently no treatment for ARID1B-related intellectual disability. The aim of this study is to assess the efficacy and safety of clonazepam in patients with ARID1B-related intellectual disability.

Study objective

• clonazepam administration has acute beneficial effects compared
to placebo on neurocognitive tests.
• multiple-doses clonazepam has beneficial effects compared to placebo on behaviour and cognitive function in ARID1B patients as measured by the ABC, and CGI-I scale.

Study design

-28 Days till EOS

Intervention

Clonazepam and placebo

Contacts

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Eligibility criteria

Inclusion criteria

Part A, correlation blood-saliva PK.
• Healthy male or female volunteers aged 18-30 years
• Informed consent provided by volunteer

Part B: ARID1B patients.
• Informed consent provided by both parents, or the legal guardian prior to any study mandated procedure.
• Known mutation in ARID1B
• Assent provided by the participant.

• Aged 6 years or older
• Able to perform at least 5 of the 6 NeuroCart® activities.

Exclusion criteria

Part A, healthy volunteers
• Disorder that could interfere with saliva production.
• Known hypersensitivity to clonazepam, other benzodiazepines or other excipients of the study medication.
• Treatment with another investigational drug within 3 months prior to screening or more than 4 times a year.
• History or clinical evidence of any disease and/or existence of a surgical or medical condition which might interfere with the absorption, distribution, metabolism or excretion of the study drug.
• History of severe respiratory problems or severe liver- or renal insufficiency.
• Other medical or psychosocial history making the participant unsuitable for participation as determined by the treating paediatrician.
• History or clinical evidence of alcoholism within the 3-year period prior to screening (i.e. regular use of more than 21 units of alcohol/week).
• Clinically significant findings on physical examination.
• Medications with a strong influence on CYP3A4 metabolism
• Clinically meaningful blood loss (including blood donation), or a transfusion of any blood product within 12 weeks before screening.
• Subjects with a BMI > 30 and/or cardiovascular, respiratory or immune system disorders

Part B: ARID1B patients.
• Clear indication of not wanting to participate during the study
• Use of benzodiazepines or any other medication or drug with the potential to influence study related endpoints in the investigator’s opinion (including e.g. CYP3A4-related drugs).
• Known hypersensitivity to clonazepam, other benzodiazepines or other excipients of the study medication.
• History of severe respiratory problems or severe liver- or renal insufficiency.
• Other medical or psychosocial history making the participant unsuitable for participation as determined by the treating paediatrician.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2020
Enrollment:	40
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Plan description
N.A.

Ethics review

Positive opinion

Date:	23-07-2020
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 52899
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL8792
CCMO	NL71395.056.19
OMON	NL-OMON52899

Study results

Summary results
N.A.