Clonazepam in ARID1B Evaluation (CARE study)

Gepubliceerd: 23-07-2020 Laatst bijgewerkt: 15-05-2024

• 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...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON29120

Bron
NTR

Verkorte titel
CHDR1939

Aandoening

ARID1B

Ondersteuning

Primaire sponsor: CHDR
Overige ondersteuning: CHDR

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

• 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.

Onderzoeksopzet

-28 Days till EOS

Onderzoeksproduct en/of interventie

Clonazepam and placebo

Contactpersonen

Publiek

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-04-2020
Aantal proefpersonen:	40
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Toelichting
N.A.

Ethische beoordeling

Positief advies

Datum:	23-07-2020
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 52899
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten
N.A.