Ambroxol in Gaucher disease 3: n-of-1 series

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Based on previous studies, we will expect that ambroxol improves neurological manifestations in patients with GD3.

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON20818

Bron
NTR

Verkorte titel
The ATTACK-GD3 study

Aandoening

Gaucher disease type 3

Ondersteuning

Primaire sponsor: MetaKids, Vriendenloterij
Overige ondersteuning: -

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Change in cerebrospinal fluid (CSF) Lyso-GL1, from GD3 patients receiving ambroxol.

Toelichting onderzoek

Achtergrond van het onderzoek

Gaucher disease (GD) is an autosomal recessive lysosomal storage disease (LSD), caused by bi-allelic mutations in GBA1 resulting in a deficiency of the lysosomal enzyme glucocerebrosidase (GCase). GD is biochemically characterized by lysosomal accumulation of glucosylceramide (GL-1) and its deacylated form, glucosylsphinogosine (Lyso-GL1). Clinically, GD is classified intro three subtypes (GD1-3). All present with multisystemic disease manifestations (i.e. enlarged liver and spleen, anaemia). GD2 and GD3 are less common and include involvement of the central nervous system (CNS). GD3 patients present with untreatable progressive neurodegenerative disease, i.e. progressive developmental delay, myoclonic epilepsy, supranuclear gaze palsy and ataxia. The systemic manifestations of GD can be treated by enzyme replacement therapy (ERT). However, ERT is not able to cross the blood-brain barrier (BBB) and hence no treatment for the devastating neurological symptoms is available. Ambroxol is a small molecule chaperone that has been shown to increase GCase activity in vitro and is able to cross the BBB. Because classical randomized controlled trials (RCTs) are unfit to perform due to a low prevalence and heterogeneity of GD3, we will combine the results of several n-of-1 trials. The purpose of this study is to evaluate the neurological efficacy of ambroxol in patients with GD3, using an n-of-1 series.

Doel van het onderzoek

Based on previous studies, we will expect that ambroxol improves neurological manifestations in patients with GD3.

Onderzoeksopzet

Outcome measures will be assessed during the baseline period and during the whole trial period every 3 or 6 months. A follow-up visit will be scheduled 6 weeks and 3 months after the end of the trial.

Onderzoeksproduct en/of interventie

Each patient receives multiple blocks consisting of three time daily ambroxol (25 mg/kg/day) alternated with placebo and washout periods.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1) The patient or the parent(s)/legal guardian(s) must provide written informed consent before start of the study
2) Male and female patients with documented deficiency of GCase activity and GBA genotype fitting GD3
3) All ages
4) Able to travel to the study site
5) Patients receive ERT with treatment ongoing at the time of enrollment
6) There are no sufficient data for the use of ambroxol in pregnant women (see Summary of product characteristics (SPC), section 4.6). This particularly concerns the period up to the 28th week of pregnancy. Postmenarchal female patients must be willing to practice true abstinence in line with their preferred and usual lifestyle, or use a medically accepted form of contraception throughout the study (barrier method such as condom or diaphragm+spermicide or non-barrier method such as oral, injected, or implanted hormonal contraceptive with ethinylestradiol and norethindrone or similar active components

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1) The patient is transfusion dependent
2) The patient has received an investigational product within 30 days prior to enrollment
3) Known hypersensitivity reactions, intolerance or adverse reactions to ambroxol or to the inactive ingredients
4) The patient is lactating. Ambroxol crosses into the breast milk. As there is no adequate experience in humans to date, ambroxol should not be used in lactation in a study setting (see SPC, section 4.6)
5) Pregnancy

6) The patient is unwilling or, in the investigator’s opinion, unable to adhere to the requirements of the study
7) The patient is unable to swallow powder and has no other enteral access (e.g. gastrostomy)
8) Any condition or abnormality which may, in the opinion of the investigator, compromise the safety of patients

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	03-01-2022
Aantal proefpersonen:	4
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9550
Ander register	METC AMC : METC 2021_152

Resultaten