An observational, prospective, multi-centre, natural history study of patients with mucopolysaccharidosis type IIIA

Published: 23-05-2016
Last updated: 17-04-2024

Evaluate the clinical progression in patients with MPS IIIA who are untreated with any investigational product and to obtain standardized assessments: neurocognitive, behavioural, sleep-wake habits and effect of MPS IIIA on the quality of life of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Observational non invasive

Summary

ID

NL-OMON46191

Source
ToetsingOnline

Brief title
Natural history study of patients with MPS IIIA

Condition

- Chromosomal abnormalities, gene alterations and gene variants

Synonym
or Mucopolysaccharidosis type III (MPS III), Sanfilippo syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Lysogene SA
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Lysosomal disease, MPS IIIA, Mucopolysaccharidosis type IIIA, Sanfilippo syndrome

Outcome measures

Primary outcome

Study endpoints:

1. The change from baseline in cognitive function using the Bayley scales of infant and toddler development third edition

2. The change from baseline in the adaptive behaviour composite standard score as measured by the Vineland Adaptive Behaviour Scales, second edition - Expanded interview (VABS-II)

3. Longitudinal description of sleep disturbances in MPSIIIA children using the Children*s sleep habits questionnaire, diary and Actigraphy

4. A description of the patient and parents quality of life

5. A description of the adverse events

6. The change from baseline in total cortical grey matter volume will be recorded, ONLY if brain MRI is standard of care

7. Concentrations of biomarkers will be studied, ONLY if drawing blood/lumbar puncture is standard of care

Secondary outcome

Non Applicable

Study description

Background summary

Sanfilippo syndrome, or Mucopolysaccharidosis type III (MPS III), is a rare lysosomal disease. MPS IIIA is caused by an autosomal recessive genetic defect of a lysosomal sulfamidase. MPS IIIA is a rare disease with an estimated prevalence of approximately 1 per 100,000 live birth. Clinical manifestations are predominantly characterized by severe neurodegenerative features combined with relatively milder somatic symptoms. It leads to an extremely deteriorated quality of life and is a particularly devastating disease both for those affected and their families. There is variability in the disease phenotype but not a fully predictive genotype-phenotype correlation. A majority (70%) of patients are reported to have the severe classical form of MPS IIIA. The median age of death is about 15 years of age .
The most commonly reported cause of death is pneumonia. There is currently no disease altering treatment for MPSIIIA. Lysogene is developing a gene therapy intended to be a one-time treatment for MPS IIIA. Lysogene*s gene therapy route of administration is direct delivery of the vector to the CNS. This may be one of the most efficient methods to treat neurological pathologies of LSDs.
Lysogene is planning a multi-centre pivotal phase II/III study in around 20 patients in Europe and the USA.
For more information, you can go to the protocol section "Background" p14/66.

Study objective

Evaluate the clinical progression in patients with MPS IIIA who are untreated with any investigational product and to obtain standardized assessments: neurocognitive, behavioural, sleep-wake habits and effect of MPS IIIA on the quality of life of patients and their families. To assess the cross-reactive immunological material status of MPSIIIA patients.

Study design

This is a European, multi-centre, prospective, descriptive cohort study to detail the natural course of MPSIIIA via standardized clinical, biochemical, neurocognitive, developmental, and behavioural measures.
This study will have up to 6 onsite visits as follows:
Screening
Baseline (assessment day 0)
Assessment: 6-month contact (+/-14 days) from baseline
Assessment: 12-month contact (+/-14 days) from baseline
Assessment: 18-month contact (+/-14 days) from baseline
Assessment: 24-month contact (+/-14 days) or end of study visit from baseline

Study burden and risks

Potential benefits (protocol p15/66): Participants will have access to routine metabolic follow up that may improve medical care. They will have neuropsychological testing performed that may assist in educational

planning.This natural history should provide important information about the clinical course of MPS IIIA. The information to be learned should be useful in understanding future therapeutic effects.

Contacts

Public
Lysogene SA

Jacques Dulud 18-20
Neuilly sur Seine 92200
FR
Scientific
Lysogene SA

Jacques Dulud 18-20
Neuilly sur Seine 92200
FR

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

* Documented MPS IIIA diagnosis.
* Children up to and including 9 years of age.
* The patient is sufficiently able, in the opinion of the Investigator, to adhere to the study visit schedule and other protocol requirements.
* The patient's parent(s) or legal guardian(s) has signed written informed consent, according to the local regulations and after all relevant aspects of the study have been explained and discussed.

Exclusion criteria

* The patient is participating in a clinical trial of any potential disease-modifying investigational medicinal product or taking high dose (>100 mg/kg/day) synthetic Genistein (patients on low dose or naturally derived genistein can be included in this study).
* The patient has received a hemapoietic stem cell or bone marrow transplant or gene therapy.
* The patient has received enzyme replacement therapy.
* Homozygous or compound heterozygous for the S298P mutation or the investigator and/or trial steering committee considers the patient not to have the classical severe form of MPS IIIA.
* Individuals with rare and unrelated serious comorbidities e.g. Down syndrome, intraventricular haemorrhage in the new-born period, or extreme low birth weight (<1500 grams).
* Visual or hearing impairment sufficient, in the clinical judgment of the investigator, to preclude cooperation with neurodevelopmental testing. Use of hearing aids is permitted.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-07-2016
Enrollment:	5
Type:	Actual

Ethics review

Approved WMO

Date:	23-05-2016

Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL56624.018.16
Other	The protocol will be registered on clinicaltrials.gov