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Efficacy and safety of enzyme replacement therapy for Mucopolysaccharidosis type I with 100 IU/Kg recombinant human a-L-iduronidase (Aldurazyme™)

Submission date	Recruitment status	[ ] Prospectively registered
06/03/2007	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
06/03/2007	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
20/08/2021	Nutritional, Metabolic, Endocrine	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
NL331 (NTR369)

Study information

Scientific Title
Efficacy and safety of enzyme replacement therapy for MPS I with 100 I.U./Kg recombinant human a-L-iduronidase (ALDURAZYME™).

Study objectives
Mucopolysaccharidosis type I (MPS I) is caused by the deficiency of the lysosomal enzyme a-L-Iduronidase. Due to this deficiency heparan sulphate and dermatan sulphate (Glycosaminoglycans [GAGs]) accumulate in the lysosomes of all cells, but predominantly in the connective tissue. Clinical features encompass a spectrum of disease manifestations. Three phenotypes are recognised:
1. The neuronopathic (Hurler) type at one end of the spectrum
2. An intermediate (Hurler-Scheie) phenotype
3. A non-neuronopathic (Scheie) phenotype at the far end of the spectrum

In both the non-neuronopathic and neuronopathic forms, visceral complications occur, such as joint abnormalities, hepatomegaly, cardiac valve abnormalities, skeletal abnormalities and corneal clouding. The most severe expression of the disease is found in the neuronopathic form; here visceral symptoms occur very early in life, with concomitant devastating, irreversible central nervous system involvement, giving rise to considerable morbidity from a very early age onwards and death on average around the fifth year of age.

In the Scheie phenotype psychomotor development is normal. Skeletal and joint manifestations form the important disease burden in these patients. Recently, trials with weekly a-L-Iduronidase (Aldurazyme™, Genzyme/Biomarin) infusions showed improvement in joint mobility, lung function and exercise tolerance, as determined by the six minute walk test. Aldurazyme™ received marketing approval as an orphan drug from the European Medicines Agency (EMEA) in April 2003. However, there are still many open issues regarding the efficacy of treatment, making uniform evaluation of treatment in selected groups of MPS I patients mandatory.

Hypothesis:
MPS I patients can be treated with Aldurazyme safely and effectively.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the local medical ethics committee

Study design
Non-randomised, non-controlled, parallel group, multicentre clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Mucopolysaccharidosis type I

Interventions

Enzyme replacement therapy with Aldurazyme™.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Recombinant human a-L-iduronidase (Aldurazyme™)

Primary outcome(s)
1. Improvement of joint mobility
2. Improvement of quality of life

Key secondary outcome(s))
1. Improvement of sleep apnea registration
2. Improvement in six-minute walk test
3. Improvement of cardiac geometry and function
4. Improvement in lung function
5. Improved motor performance (handicap status)
6. Evaluation of visual acuity/performance
7. Evaluation of mental condition and social performance
8. Decrease of liver and/or spleen size as measured by ultrasound
9. Effect of dose and infusion rate on plasma enzyme levels and enzyme availability

Completion date
31/12/2005

Eligibility

Key inclusion criteria
1. The patient must give written informed consent
2. If the patient is younger than 12 years, informed consent from his/her parents or his/her legal representative is necessary
3. If the patient is below 18 years, but older than 12 years, informed consent from the child is necessary if the patient is mentally and physically able to do so
4. The patients can be included in this protocol, and not in any of the two other MPS I treatment protocols
5. The patient must have a current diagnosis of MPS I, as documented by a decreased a-L-iduronidase activity in leukocytes or fibroblasts
6. Patients must be willing and able to comply with the study protocol
7. Female patients must have a negative pregnancy test, and must use a medically accepted method of contraception during the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Sex
All

Key exclusion criteria
1. Patient is unable or unwilling to comply with the study protocol
2. Parent(s) or legal representatives are unable or unwilling to comply with the evaluation program
3. Patient is pregnant or lactating
4. Life expectancy less than six months
5. Very severe neurological involvement as evidenced by:
a. total or subtotal absence of cortical activity (vegetative state)
b. untreatable seizures
c. loss of (almost) all abilities to communicate

Date of first enrolment
01/01/2004

Date of final enrolment
31/12/2005

Locations

Countries of recruitment
Netherlands

Study participating centre
Erasmus Medical Centre Rotterdam
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Sponsor information

Organisation
Erasmus Medical Centre (The Netherlands)

ROR
https://ror.org/018906e22

Funder(s)

Funder type
Government

Funder Name
Dutch Health Care Insurance Board (College Voor Zorgverzekeringen [CVZ]) (The Netherlands)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration