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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

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

### Secondary identifying numbers
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

### Secondary study design

Multi-centre

### Study setting(s)
Hospital

### Study type(s)
Treatment

### Participant information sheet

### 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 measure
1. Improvement of joint mobility
2. Improvement of quality of life

### Secondary outcome measures
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

### Overall study start date
01/01/2004

### 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

### Age group
Child

### Sex
Both

### Target number of participants
35

### 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)

**Sponsor details**
Sophia Children's Hospital
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**Sponsor type**
Hospital/treatment centre

**Website**
http://www.erasmusmc.nl/

**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

**Publication and dissemination plan**
Not provided at time of registration

**Intention to publish date**

## Individual participant data (IPD) sharing plan

### IPD sharing plan summary
Not provided at time of registration