A Study to Assess the Safety and Tolerability of SOBI003 in Pediatric MPS IIIA Patients

ClinicalTrials.gov Identifier: NCT03423186

Recruitment Status : Completed
First Posted : February 6, 2018
Last Update Posted : May 13, 2020

Sponsor:
Swedish Orphan Biovitrum

Information provided by (Responsible Party):
Swedish Orphan Biovitrum

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

Study Description

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Brief Summary:
MPS IIIA, also known as Sanfilippo A, is an inherited lysosomal storage disease (LSD). MPS IIIA is caused by a deficiency in sulfamidase, one of the enzymes involved in the lysosomal degradation of the glycosaminoglycan (GAG)

heparan sulfate (HS). The natural course of MPS IIIA is characterized by devastating neurodegeneration with initially mild somatic involvement. The aims of the present study is to assess the dose related safety, tolerability, PK and PD of **SOBI**003, a chemically modified recombinant human (rh) Sulfamidase developed as an enzyme replacement therapy (ERT).

Condition or disease	Intervention/treatment	Phase
Sanfilippo Syndrome Type A (MPS IIIA)	Drug: **SOBI**003	Phase 1 Phase 2

Detailed Description:
This is an open-label, non-controlled, parallel, sequential ascending multiple-dose, multicenter study to assess the dose related safety, tolerability, PK and PD of SOBI003 in pediatric MPS IIIA patients. Patients between 1 and 6 years of age who have not received previous treatment for MPS IIIA with an ERT, gene- or stem cell therapy will be eligible to participate in the study. The study is planned to consist of 3 dose cohorts, each comprising 3 patients. Treatment initiations will be staggered within each cohort in order to be able to observe, interpret and treat possible adverse reactions. SOBI003 is administered as weekly i.v. infusions over a period of 24 weeks. Upon completion of the 24-week treatment period with satisfactory tolerability, the patient is offered to receive continued SOBI003 treatment by participation in an extension study.

Study Design

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Study Type :
Interventional (Clinical Trial)

Actual Enrollment :
6 participants

Allocation:
Non-Randomized

Intervention Model:
Parallel Assignment

Masking:
None (Open Label)

Primary Purpose:
Treatment

Official Title:
An Open, Non-controlled, Parallel, Ascending Multiple-dose, Multicenter Study to Assess Safety and Tolerability, Pharmacokinetics and Pharmacodynamics of **SOBI**003 in Pediatric MPS IIIA Patients

Actual Study Start Date :
June 19, 2018

Actual Primary Completion Date :

October 25, 2019

Actual Study Completion Date :

October 25, 2019

Resource links provided by the National Library of Medicine

MedlinePlus Genetics related topics: Mucopolysaccharidosis type III

Genetic and Rare Diseases Information Center resources: Mucopolysaccharidosis Type III Mucopolysaccharidosis Type IIIA Mucopolysaccharidosis

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: Dose group 1 **SOBI**003 dose 3 mg/kg once weekly for 24 weeks	Drug: **SOBI**003 Weekly i.v.infusion Other Name: Modified recombinant human sulphamidase
Experimental: Dose group 2 **SOBI**003 dose 10 mg/kg once weekly for 24 weeks	Drug: **SOBI**003 Weekly i.v.infusion Other Name: Modified recombinant human sulphamidase
Experimental: Dose group 3 **SOBI**003 dose to be decided once weekly for 24 weeks	Drug: **SOBI**003 Weekly i.v.infusion Other Name: Modified recombinant human sulphamidase

Outcome Measures

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Primary Outcome Measures :

1. Safety will be measured by adverse events frequencies (by type and severity) [Time Frame: Week 24]

Secondary Outcome Measures :

1. The observed serum concentration immediately before the start of infusion of **SOBI**003 (CPre-dose) [Time Frame: Weeks 1, 2, 3, 4, 5, 8, 12, and 24]
2. The observed serum concentration at the end of infusion of **SOBI**003 (CEnd of inf) [Time Frame: Weeks 1, 2, 3, 4, 8, 12, and 24]
3. The time of the end of the infusion of **SOBI**003 (tEnd of inf) [Time Frame: Weeks 1, 2, 3, 4, 8, 12, and 24]
4. The maximum observed serum concentration (Cmax) [Time Frame: Weeks 1, 4, 12, and 24]
5. The time at which the maximum serum concentration is observed (tmax) [Time Frame: Weeks 1, 4, 12, and 24]
6. The minimum observed serum concentration (CTrough) [Time Frame: Weeks 1, 4, 12, and 24]
7. Clearance (CL) [Time Frame: Weeks 1, 4, 12, and 24]
8. The area under the plasma concentration-time curve from time 0 to last sample (AUC0-168h) [Time Frame: Weeks 1, 4, 12, and 24]
9. The half-life (t1/2) [Time Frame: Weeks 1, 4, 12, and 24]
10. **SOBI**003 concentration in cerebrospinal fluid [Time Frame: Weeks 12 and 24]
11. Proportion of patients having anti-drug antibodies in serum [Time Frame: Weeks 2,4,8,12 and 24]
12. Proportion of patients having anti-drug antibodies in cerebrospinal fluid [Time Frame: Weeks 2,4,8,12 and 24]
13. Change from baseline in Heparan Sulfate levels in cerebrospinal fluid [Time Frame: Weeks 12 and 24]
14. Change from baseline in Heparan sulfate levels in serum [Time Frame: Weeks 2, 3, 4, 8, 12 and 24]
15. Change from baseline in Heparan sulfate levels in urine [Time Frame: Weeks 2, 3, 4, 8, 12 and 24]
16. Change from baseline in Neurocognitive Development Quotient [Time Frame: Week 24]

    Quotient between age equivalent score and age, 0 - 100%, where high values are desirable. The age equivalent score represent the age of the typical and normal individual who would achieve the same result as the one who was tested.

    The age equivalent scores are assessed by the Bayley Scales of Infant and Toddler Development®, third edition cognitive subtest or the Kaufman Assessment Battery for Children, Second edition.

    The Bayley Scales of Infant and Toddler Development-Third Edition is an individually administered test designed to assess developmental functioning of infants and toddlers. The Bayley-III assesses development in five areas: cognitive, language, motor, social-emotional, and adaptive behavior.

The Kaufman Assessment Battery for Children (K-ABC) is a clinical instrument for assessing cognitive development.

17. Change from baseline in Age-equivalence score as assessed by BSID-III or KABC-II [Time Frame: Week 24]

    The age equivalent score represent the age in months of the typical and normal individual who would achieve the same result as the one who was tested.

    The age equivalent scores are assessed by the Bayley Scales of Infant and Toddler Development®, third edition cognitive subtest or the Kaufman Assessment Battery for Children, Second edition.

    The Bayley Scales of Infant and Toddler Development-Third Edition is an individually administered test designed to assess developmental functioning of infants and toddlers. The Bayley-III assesses development in five areas: cognitive, language, motor, social-emotional, and adaptive behavior.

    The Kaufman Assessment Battery for Children (K-ABC) is a clinical instrument for assessing cognitive development.

18. Change from baseline in Age-equivalence score as assessed by VABS-II [Time Frame: Week 24]

    The age equivalent score represent the age in months of the typical and normal individual who would achieve the same result as the one who was tested.

    The age equivalent scores are assessed by Vineland™ Adaptive Behavior Scales, Expanded Interview Form, Second edition (VABS-II). The Vineland is designed to measure adaptive behavior of individuals from birth to age 90.

    The Vineland-II contains 5 domains each with 2-3 subdomains. The main domains are: Communication, Daily Living Skills, Socialization, Motor Skills, and Maladaptive Behavior.

19. Change from baseline in gray matter volume [Time Frame: Week 24]

    Grey matter contains most of the brain's neuronal cell bodies. The grey matter includes regions of the brain involved in muscle control, and sensory perception such as seeing and hearing, memory, emotions, speech, decision making, and self-control. The gray matter volume will be measured by volumetric magnetic resonance imaging (MRI).

20. Change from baseline in Pediatric Quality of Life Inventory (PedsQL™) total score [Time Frame: Week 24]

    Pediatric Quality of Life Inventory (PedsQL™) is a modular approach to measuring health-related quality of life (HRQOL) in healthy children and adolescents and those with acute and chronic health conditions. Lower scores indicate better functioning. Min score = 0, and max score = 144.

21. Change from baseline in PedsQL™ Family Impact Module total score [Time Frame: Week 24]

    Pediatric Quality of Life Inventory (PedsQL™) is a modular approach to measuring health-related quality of life in healthy children and adolescents and those with acute and chronic health conditions. The Total Score is the sum of all 36 items in the test divided by the number of items answered. Higher scores indicate better functioning.

Eligibility Criteria

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Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:

12 Months to 72 Months (Child)

Sexes Eligible for Study:

All

Accepts Healthy Volunteers:

No

Criteria

Inclusion Criteria:

1. Informed consent obtained from the patient's legally authorized representative(s)
2. Patients with MPS IIIA, as confirmed by both:
   - A documented deficiency in sulfamidase enzyme activity in concordance with a diagnosis of MPS IIIA, and
   - Normal enzyme activity level of at least one other sulfatase measured in leukocytes
3. Chronological age of ≥12 and ≤72 months (i.e., 1 to 6 years) at the time of the first SOBI003 infusion and a developmental age ≥12 months at screening as assessed by the Vineland Adaptive Behavior Scales, Second Edition (VABS-II)
4. Medically stable patient who is expected to be able to comply with study procedures

Exclusion Criteria:

1. At least one S298P mutation in the SGSH gene
2. Contraindications for anesthetic procedures, surgical procedure (venous access port) MRI scans and/or lumbar punctures
3. History of poorly controlled seizures
4. Patients is currently receiving psychotropic or other medications which in the investigator's opinion, would be likely to substantially confound test results
5. Significant non-MPS IIIA-related CNS impairment or behavioral disturbances, which in the investigator's opinion, would confound the scientific integrity or interpretation of study assessments
6. Prior administration of stem cell or gene therapy, or ERT for MPS IIIA
7. Concurrent or prior (within 30 days of enrolment into this study) participation in a study involving invasive procedures

Contacts and Locations

Go to

Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT03423186***

Locations

United States, California

Childrens's Hospital and Research Center
Oakland, California, United States, 94609

United States, North Carolina

University of North Carolina Hospitals
Chapel Hill, North Carolina, United States, 27599

Germany

University Medical Center Hamburg-Eppendorf
Hamburg, Germany

Turkey

Gazi University Hospital
Ankara, Turkey

Sponsors and Collaborators

Swedish Orphan Biovitrum

Investigators

Principal Investigator: Paul Harmatz, MD Childrens's Hospital and Research Center Oakland

More Information

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Responsible Party:
Swedish Orphan Biovitrum

ClinicalTrials.gov Identifier:
NCT03423186 History of Changes

Other Study ID Numbers:
SOBI003-001

First Posted:
February 6, 2018 Key Record Dates

Last Update Posted:
May 13, 2020

Last Verified:
May 2020

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD:
No

Plan Description:
Undecided

Studies a U.S. FDA-regulated Drug Product:
Yes

Studies a U.S. FDA-regulated Device Product:
No

Additional relevant MeSH terms:

Mucopolysaccharidosis III

Mucopolysaccharidoses

Carbohydrate Metabolism, Inborn Errors

Metabolism, Inborn Errors

Genetic Diseases, Inborn

Lysosomal Storage Diseases

Mucinoses

Connective Tissue Diseases

Metabolic Diseases