A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multinational Clinical Study to Evaluate the Efficacy and Safety of 2.0 mg/kg/week and 2.0 mg/kg/every other week BMN 110 in Patients with Mucopolysaccharidosis IVA (Morquio A Syndrome)

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This study will evaluate the efficacy and safety of 2.0 mg/kg/week and 2.0 mg/kg/every other week BMN 110 in patients with mucopolysaccharidosis IVA (Morquio A Syndrome). This study will compare the effects of 24 weeks of infusions of BMN 110 at...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cytoplasmic disorders congenital
Study type	Interventional

Summary

ID

NL-OMON36522

Source
ToetsingOnline

Brief title
MOR-004

Condition

- Cytoplasmic disorders congenital
- Inborn errors of metabolism

Synonym

Syndrome of Morquio

Research involving
Human

Sponsors and support

Primary sponsor: BioMarin
Source(s) of monetary or material Support: BioMarin Pharmaceutical Inc.

Intervention

Keyword: Lysosomal Storage Disorder, MOR-004, Morquio Syndrome, Mucopolysaccharidosis IV A

Outcome measures

Primary outcome

The primary endpoint of this trial is to evaluate the ability of 2.0 mg/kg/week BMN 110 and 2.0 mg/kg/qow BMN 110 compared with placebo to enhance endurance in patients with MPS IVA, as measured by an increase in the number of meters walked in the 6-minute walk (6MW) test from baseline to Week 24.

Secondary outcome

The secondary objectives of the study are:

* To evaluate the ability of 2.0 mg/kg/week BMN 110 and 2.0 mg/kg/qow BMN 110 compared with placebo to enhance endurance in patients with MPS IVA, as measured by an increase in the number of stairs climbed per minute in the 3MSC test from baseline to Week 24.

* To evaluate the ability of 2.0 mg/kg/week BMN 110 and 2.0 mg/kg/qow BMN 110 compared with placebo to reduce urine KS levels in patients with MPS IVA, as measured by a decrease in urine KS levels from baseline to Week 24.

Study description

Background summary

Mucopolysaccharidosis IVA (Morquio A syndrome, MPS IVA) is an inherited autosomal recessive disorder characterized by deficient activity of N-acetylgalactosamine-6-sulfatase (GALNS), resulting in macroscopic accumulation of the glycosaminoglycan (GAG) keratan sulfate (KS) in tissue macrophages, hyaline cartilage and other connective tissues, heart valve, and cornea as well as excretion in the urine. This accumulation causes multiple clinical manifestations including impaired functional capacity, endurance, and quality of life. There is currently no standard accepted treatment for MPS IVA other than supportive care. Enzyme replacement therapy (ERT) with BMN 110 (rhGALNS) may be a potential new treatment option for MPS IVA patients. BMN 110 is expected to reduce the progressive accumulation of KS and improve signs and symptoms of the disease. This study will compare the effects of 24 weeks of infusions of BMN 110 at doses of 2.0 mg/kg/week and 2.0 mg/kg/every other week (qow) with placebo in patients with MPS IVA.

Study objective

This study will evaluate the efficacy and safety of 2.0 mg/kg/week and 2.0 mg/kg/every other week BMN 110 in patients with mucopolysaccharidosis IVA (Morquio A Syndrome). This study will compare the effects of 24 weeks of infusions of BMN 110 at doses of 2.0 mg/kg/week and 2.0 mg/kg/every other week (qow) with placebo in patients with MPS IVA.

Study design

This is a Phase 3, randomized, double-blind, placebo-controlled, multinational study in patients with MPS IVA. Eligible patients will be randomized 1:1:1 to the 2.0 mg/kg/week BMN 110 group, the 2.0 mg/kg/qow BMN 110 group, or the placebo control group. All patients will receive weekly double-blind infusions of 2.0 mg/kg/week BMN 110, 2.0 mg/kg/qow BMN 110 and infusions of placebo on alternating weeks, or placebo for a total of 24 consecutive weeks. As patients may experience hypersensitivity reactions associated with the administration of BMN 110, antihistamine will be administered prior to infusions for all patients. Pretreatment with an antipyretic may be given at the Investigator*s discretion. Vital signs will be measured just before, during, and immediately following the infusion. Adverse events and changes in concomitant medication will be recorded throughout the study. All patients who participate in this study will be eligible to receive BMN 110 in an extension study.

Intervention

Patients randomized to active treatment will receive intravenous (IV) infusions of BMN 110 at a dose of 2.0 mg/kg/week or infusions of BMN 110 at a dose of 2.0 mg/kg/qow. Patients randomized to the 2.0 mg/kg/qow arm will receive infusions of placebo on alternating weeks. Each infusion will be administered over a period of approximately 4 hours once a week for 24 consecutive weeks. Patients randomized to placebo will receive weekly IV infusions of placebo solution at a volume equivalent to that needed for a 2.0 mg/kg dose of BMN 110. BMN 110 as well as placebo should be diluted in 0.9% sodium chloride.

Study burden and risks

All of the possible risks from treatment with BMN 110 are unknown. BMN 110 has been tested in animals and has also been used in a small group of patients with MPS IVA in another clinical study. The most common side effects seen in the clinical study so far have been mild or moderate and include cough, fever, vomiting, headache, and pain in arms or legs.Allergic Reactions: As with any drug, it is possible that patients could experience an allergic reaction to any of the drugs or combination of the drugs used in this study. Symptoms of any allergic reaction can include a rash, hives, itching, and/or difficulty breathing, closing of the throat, swelling of the lips, tongue or face, and rarely death. When a X-ray is performed, the patient will be exposed to a small amount of radiation. Risks associated with drawing blood include: possibility of discomfort while the blood is being drawn or for a short time afterward, possibility of bruising or bleeding at the needle puncture site, and rarely, infection at the needle puncture site. Other possible side effects from blood draws include lightheadedness and/or fainting. Risks of the physical endurance tests: The effects of the study drug and some study procedures on a fetus or baby are unknown. Females who are sexually active and/or are capable of becoming pregnant must either (a) not have sex or (b) use birth control for 30 days after taking study drug. Like any other experimental drug, this study drug may have unknown and serious risks that could lead to death. Study procedures may involve risks or side effects that are not known because of MPS IV A. Also, things could happen that the doctors don*t know about yet.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

* At least 5 years of age.
* Documented clinical diagnosis of MPS IVA based on clinical signs and symptoms of MPS IVA and documented reduced fibroblast or leukocyte GALNS enzyme activity or genetic testing confirming diagnosis of MPS IVA.
* Willing and able to provide written, signed informed consent, or in the case of patients under the age of 18 (or 16 years, depending on the region), provide written assent (if required) and written informed consent by a legally authorized representative after the nature of the study has been explained, and prior to any research-related procedures.
* Must have an average screening 6MW test distance * 30 and * 325 meters.
* Sexually active patients must be willing to use an acceptable method of contraception while participating in the study.
* Females of childbearing potential must have a negative pregnancy test at Screening and be willing to have additional pregnancy tests during the study.

Exclusion criteria

* Previous hematopoietic stem cell transplant (HSCT).
* Previous treatment with BMN 110.
* Has known hypersensitivity to any of the components of BMN 110.

* Major surgery within 3 months prior to study entry or planned major surgery during the 24-week treatment period.
* Pregnant or breastfeeding at Screening or planning to become pregnant (self or partner) at any time during the study.
* Use of any investigational product or investigational medical device within 30 days prior to Screening, or requirement for any investigational agent prior to completion of all scheduled study assessments.
* Concurrent disease or condition, including but not limited to symptomatic cervical spine instability, clinically significant spinal cord compression, or severe cardiac disease that would interfere with study participation or safety as determined by the Investigator.
* Any condition that, in the view of the Investigator, places the patient at high risk of poor treatment compliance or of not completing the study.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-05-2011
Enrollment:	7
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Not Applicable
Generic name:	Not Applicable

Ethics review

Approved WMO Date:	08-02-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-08-2011
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
EudraCT	EUCTR2010020198-18-NL
CCMO	NL34445.018.11