A Multicenter, Multinational, Extension Study to Evaluate the Long-Term Efficacy and Safety of BMN 110 in Patients with Mucopolysaccharidosis IVA (Morquio A Syndrome)

Published: 25-07-2011
Last updated: 29-04-2024

To evaluate the long-term safety and efficacy of BMN 110 administration at 2.0 mg/kg/qw and 2.0 mg/kg/qow in patients with MPS IVA.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Cytoplasmic disorders congenital
Study type	Interventional

Summary

ID

NL-OMON35977

Source
ToetsingOnline

Brief title
MOR-005

Condition

- Cytoplasmic disorders congenital
- Inborn errors of metabolism

Synonym
MPS IVA, 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-005, Morquio Syndrome, Mucopolysaccharidosis IV A

Outcome measures

Primary outcome

The primary objective of the study is to evaluate the long-term safety and efficacy of BMN 110 administration at 2.0 mg/kg/qw and 2.0 mg/kg/qow in patients with MPS IVA. Efficacy Variables are assessed by means of endurance tests (6-minute walk (6MW) test and 3-minute stair climb (3MSC) test), urine KS concentration (normalized to creatinine), respiratory function tests, anthropometric measurements (standing height, length, sitting height, and weight) , skeletal radiographs of lumbar spine and lower extremity (lower extremity radiographs are done only for patients * 20 years of age) , MPS Health Assessment Questionnaire and audiometry examinations .

The safety variables are assessed by collecting adverse events (AEs), performing standard clinical laboratory tests (serum chemistry, hematology, and urinalysis), assessing vital signs, echocardiograms , electrocardiograms (ECGs) , performing routine physical examinations, including standard neurologic examination , concomitant medications, immunogenicity tests and cervical spine (flexion*extension) radiographs.

Secondary outcome

The exploratory objective of the study is to evaluate the long-term effect of BMN 110 administration at 2.0 mg/kg/qw and 2.0 mg/kg/qow on changes in biochemical markers of inflammation and bone and cartilage metabolism, in patients with MPS IVA. This will be assessed by blood inflammatory biomarkers and blood biochemical markers of bone and cartilage metabolism.

Study description

Background summary

Mucopolysaccharidosis IVA (Morquio A syndrome, MPS IVA) is an inherited autosomal recessive disorder characterized by deficiency of N-acetylgalactosamine-6-sulfatase (GALNS), resulting in pathologic 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. Excessive KS accumulation manifests clinically in multiple ways, including: reduced functional capacity and physical endurance, and hence impaired quality of life.
There is currently no accepted, standard treatment for MPS IVA other than supportive care. Enzyme replacement therapy (ERT) with BMN 110, or recombinant human GALNS (rhGALNS), may be a potential new treatment option for MPS IVA patients. BMN 110 is expected to reduce the progressive, pathologic accumulation of KS, and improve signs and symptoms of the disease.
The rationale for this phase 3 extension study is to provide patients who complete the MOR-004 study with the option to receive BMN 110 treatment. Initially, patients previously randomized to BMN 110 in the MOR-004 study will remain on their double-blind dose regimen, and patients randomized to placebo in MOR-004 will be re-randomized to receive weekly double-blind BMN 110 treatment, either qw or qow. Once an optimal BMN 110 dosing regimen has been identified (based on the final primary efficacy results of the MOR-004 study), the MOR-005 study will be unblinded and all patients will receive the optimal BMN 110 dose in an open label fashion. Long-term safety and efficacy will be

assessed in this study.

Study objective

To evaluate the long-term safety and efficacy of BMN 110 administration at 2.0 mg/kg/qw and 2.0 mg/kg/qow in patients with MPS IVA.

Study design

This is a multi-center, multinational, extension study to evaluate 2 dose regimens of BMN 110 treatment in patients with MPS IVA who completed MOR-004. The last study visit assessments for MOR-004 will constitute Baseline for this study. The first study drug dose of this protocol will occur on Week 0 of MOR-005, which is the same as the last visit (Week 24) of MOR-004. Initially, the study will be double-blind with patients previously randomized to BMN 110 in MOR-004 remaining on their assigned BMN 110 dose regimen (qw or qow dosing). The MOR-004 placebo patients will be re-randomized (1:1 ratio) to one of the 2 BMN 110 dose-regimen groups: 2.0 mg/kg/qw or 2.0 mg/kg/qow. Once the optimal dose regimen is determined from the MOR-004 study final primary efficacy and safety analysis, all patients will receive the optimum dose regimen of BMN 110 for the remainder of this study.

Intervention

During the double-blind phase of the study, patients will receive intravenous (IV) infusions of study drug at a dose of 2.0 mg/kg/qw or 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. Placebo solution will be administered IV, 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. Once the optimal dose regimen is determined from the MOR-004 study final primary efficacy and safety analysis, all patients will receive the optimum dose regimen of BMN 110 for the remainder of this study (up to Week 240).

Study burden and risks

All possible risks from treatment with BMN 110 are not yet known. BMN 110 has been tested in animals and in previous clinical trials on humans. The most common side effects seen in clinical studies so far have generally been mild or moderate and include cough, fever, vomiting, headache, and pain in arms or legs. As with any drug, it is possible that patients could experience an allergic reaction to the study drug or the combination of drugs used in this study. This mainly pertains to the patients who previously received placebo (during the MOR-004 study) and will for the first time be exposed to the study medication during this study.
Risks associated with the drawing of blood include: possibility of discomfort while the blood is being drawn or for a short time afterward, possibility of bleeding or bruising at the needle puncture site and, rarely, infection at the needle punction site. Other possible side effects from blood draws include lightheadedness and/or fainting.
The exact effects of the study drug and some study procedures on a fetus or baby are unknown. Females who are sexually active and/or fertile must either (a) not have sex or (b) use birth control during the entire study until 30 days after the last dose of study medication.
As with any experimental drug, this study may have unknown and serious risks which could even be fatal. Study procedures may also involve risks or side effects which are not known because of MPS IV A.

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

- Must have completed MOR-004.
- Is willing and able to provide written, signed informed consent. Or, in the case of patients under the age of 18 (or other age as defined by regional law or regulation), provide written assent (if required) and have written informed consent, signed by a legally authorized representative, after the nature of the study has been explained, and prior to performance of research-related procedures.
- If sexually active, must be willing to use an acceptable method of contraception while participating in the study.
- If female, of childbearing potential, must have a negative pregnancy test at Baseline and be willing to have additional pregnancy tests done during the study.

Exclusion criteria

- Pregnancy or breastfeeding, at Baseline, or planning to become pregnant (self or partner) at any time during the study.
- Use of any investigational product (other than BMN 110 in MOR-004), or investigational medical device, within 30 days prior to Baseline; or is required to use any investigational agent prior to completion of all scheduled study assessments.
- Was enrolled in a previous BMN 110 study, other than MOR-004.
- Has a 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 pose a safety risk, as determined by the Investigator.
- Has 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:	Other
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	7
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO Date:	25-07-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-04-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	28-12-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-02-2014
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	EUCTR2010-020199-45-NL
CCMO	NL37011.018.11