An open-label extension study of the long-term safety, tolerability and efficacy of drisapersen in subjects with Duchenne Muscular Dystrophy.

Published: 02-07-2015
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The purpose of this study is to assess the safety, tolerability and efficacy of long term drisapersen in subjects with DMD.

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

Summary

ID

NL-OMON43602

Source
ToetsingOnline

Brief title
Drisapersen extension study, BMN-051-302

Condition

- Muscle disorders

Synonym
Duchenne disease, Duchenne muscular dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: BioMarin
Source(s) of monetary or material Support: BioMarin (Sponsor)

Intervention

Keyword: 051-302, Drisapersen, Duchenne Muschular Dystrophy (DMD), Extension study

Outcome measures

Primary outcome

To evaluate the long-term safety and tolerability of subcutaneous or intravenous drisapersen in subjects with DMD correctable by drisapersen-induced DMD exon 51 skipping who have previously participated in an eligible study.

Secondary outcome

• To evaluate the long-term efficacy of subcutaneous drisapersen at a dose of 6 mg/kg/week.

• To evaluate the long-term impact on functional outcomes of continued treatment with drisapersen.

• To evaluate the long-term safety and efficacy of an intermittent dosing option in those subjects unable to tolerate drisapersen 6 mg/kg/week.

• To evaluate the long-term safety and efficacy of an intravenous dosing option in those subjects unable to tolerate subcutaneous administration of drisapersen.

Study description

Background summary

Duchenne Muscular Dystrophy (DMD) is the most frequent genetic moral child disease with an incidence of 1 in 3500 newborn boys. Due to the disease the cells in the muscles cannot produce the protein dystrophyn. The first signs of muscle weakness can start from the age of 2. The skeleton muscles in the arms, legs and torso will become weaker gradualy. Most of the DMD patients are in wheelchairs before they become 12 years old. Before mechanical ventilation was

introduced, most patients died around their twenties.

The disease leads to severe disability and morbitidy. Prednison is accepted to decrease the progress of the disease. However, this therapie also leads to adverse events, such as obesity, osteopenia or osteoporosis, effect on behaviour, hypertension, cataract, disturbance in growth and hormonal reactions.

Different other therapeutic strategies have been under research without succes, such as muscle cell and stam cell transplants, mediations and genetic therapies.

Antisense exon skipping is a new, promissing way to induce the amount of dystrophyn in the muscles, similar like patients with Becker muscular dystrophy. This would decrease the progression of DMD or maybe could even stop the progression.

In this study, drisapersen (BMN051) will be researched, a antisense oligonucleotide which skips exon 51. Information about earlier studies with this medication will be available in the study protocol and in the Investigator's Brochure.

Study objective

The purpose of this study is to assess the safety, tolerability and efficacy of long term drisapersen in subjects with DMD.

Study design

This is a phase IIIb, multi-centre, open-label, uncontrolled extension study in male subjects with DMD who have previously been treated with drisapersen.

This study aims to enroll up to approximately 220 subjects.

The primary dosing arm is drisapersen 6 mg/kg as subcutaneous (SC) injection(s) once a week. All subjects starting with subcutaneous injections will receive a loading dose of twice weekly 6mg/kg drisapersen for the first three weeks of treatment. This study does not have a minimum duration of participation. Subjects will have varying times of study participation depending on when they enter from one of the eligible studies and will be permitted to continue the study until such a time that they withdraw based on protocol-defined criteria, or BioMarin stops the study as described in Section 5.6 of the protocol.

For subjects who have previously experienced significant safety or tolerability issues in one of the eligible studies, or who experience these during this study, there is the potential of an alternate intermittent dosing arm. This

will be agreed in advance with the Medical Monitor.

For subjects who have previously experienced significant injection site reactions in an earlier drisapersen study, or who experience similar reaction(s) during this study, there is the potential to be dosed intravenously. IV administration may also be available for subjects based on other reasons. Studies are ongoing to determine the feasibility and safety of intravenous administration with a maximum exposure of 6 mg/kg/week over a 2 hour infusion time. Currently data is available to support IV dosing of 3mg/kg/week over a 1 hour infusion time. A switch to intravenous administration will be agreed in advance with the Medical Monitor.

Intervention

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Study burden and risks

The duration of the study is approximately 122 weeks. The patient will visit the clinic every week during this period. THe patient can be admitted to the hospital 1 time in this period for a port-a-cath(r) surgery to allow an easier access for IV administration.
The patient will be adminsterd with study drug every week, unless the patient is in the intermittent dosing arm. If the latter, the patient will be

adminstered with study drug 8 week (6mg/kg) and 4 weeks of treatment. Patients on IV treatment may receive their treatment at the daycare center during the study.

The following assessments will be performed 1 or more times during the study:

administration of drisapersen
physical examination
vital signs
ECG
Echocardiography
urine assessment
Biochemistry/hematology
bloodsamples (assessment of thrombocytes)
MRI
if necessary a skin biopt
If possible efficacy assessments: 6 minute walk test, nort start ambulatory assessment (NSAA, lung function assessment, Performance upper limb (PUL), Patient reported outcome measure (PODCI), EQ-5D-5L questionnaire.

For a detailed overview of the assesments, see appendix 1 of the protocol

Contacts

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Scientific
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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

1. Any subject who has been previously treated with drisapersen or eteplirsen
2. Continued use of glucocorticoids for a minimum of 60 days prior to study entry with a reasonable expectation that the subject will remain on glucocorticoids for the duration of this study. Changes to or cessation of glucocorticoids will be at the discretion of the investigator conducting this study in consultation with the subject/parent and Medical Monitor.

Exclusion criteria

1.Use of anticoagulants, anti-thrombotics or antiplatelet agents
2.Use of any investigatoional product within 6 months prior to the start of study (except for eteplirsen)
3.History of significant medical disorder which may confound the interpretation of safety data (e.g. current or history of renal or liver disease/impairment, history of inflammatory illness)
4.Symptomatic cardiomyopathy.
5.A platelet count under the lower limit of normal (LLN) at start of this study.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	14
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet beschikbaar
Generic name:	Drisapersen

Ethics review

Approved WMO Date:	02-07-2015
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-12-2015
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-01-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-01-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-02-2016
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2015-001955-54-NL
CCMO	NL54007.000.15