A phase II, open-label, extension study to assess the effect of PRO044 in patients with Duchenne muscular dystrophy

Published: 28-10-2014
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The objective of the study is to assess the safety, tolerability and efficacy of PRO044.

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

Summary

ID

NL-OMON41314

Source
ToetsingOnline

Brief title
PRO044-CLIN-02

Condition

- Muscle disorders

Synonym
Duchenne disease, Duchenne muscular dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Prosensa Therapeutics B.V.
Source(s) of monetary or material Support: Prosensa

Intervention

Keyword: Duchenne muscular dystrophy (DMD), exon skipping, PRO044, PRO044-CLIN-02

Outcome measures

Primary outcome

Safety, tolerability and efficacy

Secondary outcome

Pharmacokinetic profile

Study description

Background summary

Duchenne mucular dystrophy (DMD) is the most frequent genetic childhood*s disease, affecting 1 in 3500 new-born boys. Due to the disease, the muscle cells cannot produce the protein dystrophin. Patients begin to show the first signs of muscle weakness as early as the age of 2. The skeleton muscles in the arms, legs and trunk become gradually weaker. Also, the respiratory muscles and the hart become weaker from early adolescence on. Most DMD patients are often wheelchair bound before the age of 12. Before the introduction of assisted ventilation, patients died around the age of 20. The disease causes serious constrictions and morbidity. Currently, only prednisone is accepted to slow down the disease progression.
However, side effects such as overweight, osteopenia or osteoporosis, effect on behaviour, hypertension, cataract, growth retardation and hormonal problems are associated with this therapy. Other therapies have been investigated already, such as muscle cell, stem cell transplantation, drugs and gene therapy. None of these strategies seemed to be applicable in clinic.
Antisense-induced exon skipping is a new and promising approach to induce production of novel dystrophin like patients with Becker Muscular Dystrophy. This approach could strongly slow down or even stop the progression of DMD.
In this study, PRO044, an antisense oligonucleotide inducing exon 44 skipping, will be investigated. PRO044 has been shown to be effective in cultured muscle cells of DMD patients with gen deletions of exon 45 and 45-54.
The information gained from this trial (PRO044-CLIN-02) is expected to be further characterize the efficacy and safety of PRO044 over a longer treatment period of 48 weeks.

Study objective

The objective of the study is to assess the safety, tolerability and efficacy of PRO044.

Study design

Phase II, Open label extension study
2 doses (6 or 9 mg/kg); subcutaneous or intravenous

Intervention

If patient and parents consented to participate to the clinical trial, the patient will be allocated to one of the following arms:
- Weekly subcutaneous dosing with PRO044 6mg/kg
- Weekly intraveneous dosing with PRO044 6mg/kg
- Weekly intraveneous dosing with PRO044 9mg/kg

Study burden and risks

The study will last 69 weeks in total and in this period, the patient will visit the hospital 52 times. Of those 52 times, the patient will need to stay in the hospital 4 times; during these visit, PRO044 will be injected and the patients will be followed up during 24 hours.

The following treatments will be done once or several times during the study:
PRO044 administration
Physical examination
Vital signs
ECG
Echocardiography
Renal ultrasound
Urinalysis
Biochemistry/haematology
Blood drawn
MRI and MRS
Muscle biopsy
If necessary: dermatology consultation

If possible efficacy parameters: 6 minute walking distance, timed function tests, handheld myometry, North Star Ambulatory Assessment (NSAA), spirometry, performance of upper limb (PUL), Patient Reported Outcome Measure (PROM), DMD functioning and activity survey, and Egen Klassification for non-ambulant subjects.
For a more detailed overview, see Appendix 1 of the protocol (p. 68 onward)

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Inclusion criteria

1. Subjects previously treated with PRO044 in the PRO044-CLIN-01 study.;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 steroids for the duration of the study. Changes to or cessation of glucocorticoids will be at the discretion of the PI in consultation with the subject/parent and the Medical Monitor. If the subject is not on steroids, involvement in the study needs to be discussed with the medical monitor.

Exclusion criteria

1. Current or history of liver or renal disease.

2. Acute illness within 4 weeks prior to the first dose of PRO044 (Week 1) which may interfere with the measurements.
3. Severe cardiac myopathy which in the opinion of the Investigator prohibits participation in this study.
4. Need for daytime mechanical ventilation.
5. Screening aPTT above the upper limit of normal (ULN).
6. Screening platelet count below the lower limit of normal (LLN).
7. Use of anticoagulants, antithrombotics or antiplatelet agents.
8. Use of any investigational product within 6 months prior to the start of Screening for the study or during participation in the study.
9. Current or history of drug and/or alcohol abuse.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-07-2015
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	PRO044
Generic name:	PRO044

Ethics review

Approved WMO Date:	28-10-2014
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-03-2015
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-05-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-05-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-08-2015
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
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Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-11-2015
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	17-03-2016
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	EUCTR2013-003605-26-NL
ClinicalTrials.gov	NCT02329769
CCMO	NL46470.000.14