A Phase III Open Label Extension Study to Assess the Long-Term Safety and Efficacy of Idebenone in Patients with Duchenne Muscular Dystrophy (DMD) who completed the SIDEROS study

Published: 16-05-2018
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Primary:* To assess the long-term safety of idebenone in DMD patients who completed the SIDEROS study.Secondary:* To describe the long-term evolution of respiratory function in idebenone-treated DMD patients who completed the SIDEROS study,...

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

Summary

ID

NL-OMON48973

Source
ToetsingOnline

Brief title
SIDEROS-E

Condition

- Muscle disorders

Synonym
muscular dystrophy, Neuromuscular disease

Research involving
Human

Sponsors and support

Primary sponsor: Santhera Pharmaceuticals (Switzerland),
Source(s) of monetary or material Support: The research is funded by the sponsor company as described in the question B6/B7

Intervention

Keyword: Duchenne Muscular Dystrophy (DMD), Idebenone, SNT-III-012-E

Outcome measures

Primary outcome

Primary:

* Standard safety assessments, including number of premature discontinuations

of study treatment due to adverse events, incidence and severity of adverse

events, actual values and changes from baseline in safety laboratory

parameters, vital signs and electrocardiogram (ECG).

Secondary outcome

Secondary:

* Change from Baseline in Forced Vital Capacity (FVC) as percent of predicted

(FVC%p), Peak Expiratory Flow (PEF) as percent of predicted (PEF%p) and Forced

Expiratory Volume in 1 second (FEV1) as percent of predicted (FEV1%p).

Study description

Background summary

Duchenne Muscular Dystrophy is a condition that affects about 1 in every 3*000 boys. The disease affects the muscles, including
muscles involved in breathing and the heart. There is a need to develop new treatments for this disease and also to assess the
safety, tolerability and efficacy of these treatments.
Idebenone is a small molecule optimized to facilitate the transport of

electrons within mitochondria ("cellular power plants"), and
contributes to maintaining correct electron flow, which is necessary for the
production of cellular energy. Nerve and muscle cells,
including lung and heart muscle cells, are particularly energy demanding and
are, therefore, more prone to rapid loss of function
or death due to the mitochondria not producing energy properly. Through
preserving mitochondrial function and protecting cells from oxidative damage,
it is believed that idebenone can prevent cell damage and increase the
production of energy within impaired nerve and muscle tissue in DMD patients.

Study objective

Primary:
* To assess the long-term safety of idebenone in DMD patients who completed the SIDEROS study.
Secondary:
* To describe the long-term evolution of respiratory function in idebenone-treated DMD patients who completed the SIDEROS study, classified by background factors including, but not limited to age, DMD history (e.g. time of loss of ambulation, mutation type), type of steroid regimen and study treatment assignment in the SIDEROS study.

Other:
* To assess the feasibility of home-based measurement of respiratory function with hand-held nmd-1 device.
* To assess the correlation between evolution of respiratory function and clinically relevant DMD events (bronchopulmonary adverse events, use of antibiotics, hospitalizations due to respiratory system disorders, treatment interventions including assisted ventilation, reach of Peak Cough Flow (PCF) thresholds).

* To assess the correlation between evolution of respiratory function and health related quality of life outcomes for patients and caregivers.

Study design

Open-label, single-group, multi-center extension study with 4 study visits scheduled every 6 months (Visit 1/Baseline, Visit 2/Week 26, Visit 3/Week 52 and Visit 4/Week 78). Visit 8/Week 78 in SIDEROS study corresponds to SIDEROS-E Visit 1/Baseline. At the end of the SIDEROS-E study, patients will have the possibility to continue treatment with idebenone under different settings, adapted to individual countries* regulations, until the drug is commercially available for DMD indication.

Intervention

NA

Study burden and risks

Breathing tests:
For the breathing test, you will need to breathe into a special machine. You will be shown how to do it but here is a description of what to do: First you will need to take a deep breathe in and make sure that your lips are sealed around the mouthpiece. You will then need to blow out into the machine as fast as you can until your lungs are empty. How long it will take you to do this test depends on how big your lungs are but it usually takes a few seconds. You might also be asked to breathe in again and breathe out slowly for as long as you can. You might need to have a clip put on your nose so that you are not breathing out through your nose at the same time or you might need a small mask on your face if you cannot fully seal your lips on the mouthpiece.
You will be given a small machine called the nmd1 device to take home with you to use between visits. This is to measure the same things as the hospital tests measure, but at home. The respiratory therapist will show you how to use this machine. You should not feel unwell when you are doing these tests at hospital and at home but you might feel a little bit dizzy or breathless because you have been breathing so deeply. You will be allowed to have 5 minute breaks for a rest between the examinations.
The breathing tests including the home examinations with the nmd1 device are harmless and will simply measure how well and how forcefully you can breathe in and out. For the breathing tests, it is very important that you follow the instructions given by the person in charge at the hospital and in the Quick Reference Guide for the tests you do at home. The breathing tests will be done at hospital at each visit with the hospital based device and the handheld nmd1 device and at home with the nmd1 handheld device once a week until end of treatment.

Electrocardiogram (ECG)
There is one test for measuring the heart, an electrocardiogram (ECG). This test is also noninvasive and not painful. The electrocardiogram (ECG) is a tracing of your heart beating, made by recording tiny changes of electricity produced by your heart at the surface of the skin. To record these changes electrode stickers will be put on your chest with wires attached to them. It will take about 5-10 minutes. 2 ECGs will be recorded: One before you start the treatment at Visit 1 / Baseline and one when you have finished the treatment.

Blood sample analysis
Blood samples will be collected for examination at each visit. Collecting the blood samples will be the only procedure that might

cause discomfort during the study. There will be approximately 10 ml collected at each study visit, the equivalent of about 2 teaspoons. Your blood samples will be sent out of the hospital on the same day they have been collected to a central laboratory, based in the United Kingdom, for analysis. Your blood samples will be fully used to perform the analyses and will not be retained neither at the hospital neither at the central laboratory.

Benefits:
It is not yet fully known how idebenone will help your illness, but through data collected until now in previous studies, it is believed that idebenone will slow the decline of your respiratory function. Also, other people with a similar condition may benefit from the knowledge obtained from this research study. However it is not guaranteed that your participation in the study will bring you any benefit.

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

Completion of the SIDEROS study at Visit 8/ Week 78.
Signed and dated Informed Consent Form.

Exclusion criteria

Patients who discontinued SIDEROS study prematurely (i.e. did not attend all visits from V1 to V8).
Safety, tolerability or other issues arising during the course of the SIDEROS study which in the opinion of the Investigator may put the patient at significant risk or may interfere significantly with the patient's participation in the SIDEROS-E study.
Use of any investigational drug other than the study medication.

Study design

Design

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

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	04-10-2020
Enrollment:	11
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Raxone
Generic name:	Idebenone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	16-05-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	17-04-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	23-01-2020
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	28-02-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	07-09-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2017-004279-30-NL
CCMO	NL66044.058.18