Santhera (SIDEROS) [TERMINATED]

A Phase III Double-blind Study with Idebenone in Patients with Duchenne Muscular Dystrophy (DMD) taking Glucocorticoid Steroids

Hub Summary

The SIDEROS trial is designed to determine the effect of idebenone at delaying the loss of lung function in patients with DMD, receiving glucocorticoid steroids. This is a placebo-controlled trial.

Study Number: NCT02814019

Description by Santhera Pharmaceuticals

The purpose of the study is to assess the efficacy of idebenone in delaying the loss of respiratory function in patients with DMD receiving concomitant glucocorticoid steroids

The SIDEROS trial is a randomized, placebo controlled, parallel group study of the efficacy of idebenone in delaying the loss of respiratory function, whilst also monitoring safety and tolerability of idebenone in at least 266 DMD patients taking stable dose of concomitant glucocorticoid steroids.

The study treatment period will be 18 months/ 78 weeks and the idebenone dose will be 900 mg/day. Participants can use deflazacort or prednisolone and be on any dose regimen.

Since glucocorticoid steroids are widely used in ambulant boys from an early age until late into teenage and even adult years, this study will not take age and ambulatory status into account and will only exclude patients that need daytime ventilator assistance.

The schedule of assessments will include a Screening Visit and up to 9 protocol visits, including a Follow-up Visit.

A Screening Visit will take place a maximum of 6 weeks prior to the Baseline Visit (Visit 1, study day -1). Beginning at Baseline, the patient will receive study medication to be taken at home, and will undergo regular assessments in the clinic throughout the study period until Visit 8 at Week 78 at which time the study will be completed and medication discontinued.

All patients completing Visit 8/Week 78, and considered eligible by the Investigator will be able to participate in an open-label extension study (SIDEROS-E) and will continue to receive idebenone until the SIDEROS-E is terminated or Marketing Authorization is obtained for idebenone in DMD, whichever occurs first. The duration of the SIDEROS-E study will be defined in a separate protocol.

For all patients not participating in the extension study (SIDEROS-E), a Follow-up Visit (Visit 9/Follow-up Visit) will take place 4 weeks after end of Treatment at Visit 8/Week 78 or after premature discontinuation of study medication.

Each hospital visit will include efficacy assessments (respiratory function assessed by hospital-based spirometry, oxygen saturation, end-tidal CO2) and safety assessments (adverse events, concomitant medication, physical examination, vital signs and safety laboratory evaluations). In addition, respiratory function will be assessed weekly at home with a hand-held device in order to closely monitor respiratory function between hospital visits.

The study medication, all medical procedures and laboratory testing, and the visits to the study centre are free of charge. In addition, the patients will receive a travel allowance to cover reasonable expenses to and from the study centre. Participants will not otherwise be compensated for this study.

Primary Outcome Measures

- Change from baseline in forced vital capacity percent predicted (FVC %p) at week 78
- Delaying the loss of respiratory function in patients with DMD receiving glucocorticoid steroids as measured by changes in FVC %p from baseline to week 78 using hospital-based spirometry

Secondary Outcome Measures

- Change from baseline in percent predicted peak expiratory flow (PEF %p) at week 78.
- Change from baseline in forced vital capacity (FVC) at week 78.
- Change from baseline in Inspiratory flow reserve (IFR) at week 78.

Can I take part?

Inclusion Criteria

Trial Status
Trial terminated

UK Locations
London - GOSH, Trial complete/terminated, Leeds, Trial complete/terminated, Newcastle, Trial complete /terminated, Oswestry, Trial complete/terminated, Oxford, Trial complete /terminated, Queens Square, Trial complete /terminated, Temple Street, Trial complete/terminated

Trial Sponsor
Santhera Pharmaceuticals

Phase
3

Length Of Participation
18 months

Recruitment Target
266

Ambulatory
Ambulant and non-ambulant

Therapeutic Category
Respiratory/mitochondrial

Age
10 years +

Mutation Specific
Non-mutation specific therapies

Muscle Biopsy
No Muscle Biopsy Required

MRI
No

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- ✔ Male patients with a 35% FVC 80% of predicted value at Screening and at Baseline and who, in the opinion of the investigator, are in respiratory function decline phase.
- ✔ Minimum 10 years old at Screening
- ✔ Signed and dated Informed Consent Form.
- ✔ Documented diagnosis of DMD (severe dystrophinopathy) and clinical features consistent of typical DMD at diagnosis. DMD should be confirmed by mutation analysis in the dystrophin gene or by substantially reduced levels of dystrophin protein (i.e. absent or <5% of normal) on Western blot or immunostaining.
- ✔ Chronic use of systemic glucocorticoid steroids for DMD related conditions continuously for at least 12 months prior to Baseline without any dose adjustments on a mg/kg basis in the last 6 months (only dose adjustment determined by weight changes are allowed).
- ✔ Ability to provide reliable and reproducible repeat FVC values at Screening and Baselines, and reproducible within 15% (relative change) of the screening assessment at Baseline compared to Screening.
- ✔ Patients assessed by the Investigator as willing and able to comply with the requirements of the study, possess the required cognitive abilities and are able to swallow study medication.
- ✔ Patients who prior to Screening have been immunised with 23-valent pneumococcal polysaccharide vaccine or any other pneumococcal polysaccharide vaccine as per national recommendations, as well as annually immunised with inactivated influenza vaccine.

Exclusion Criteria

- ✖ Symptomatic heart failure (defined as Stage C by ACCF/AHA guideline or NYHA III-IV) and/or symptomatic ventricular arrhythmias.
- ✖ Ongoing participation in any other therapeutic trial and/or intake of any investigational drug within 90 days prior to Baseline (only exception allowed is use of Deflazacort in US as part of the Expanded Access Program).
- ✖ Prior or ongoing exon-skipping or read-through therapy for DMD.
- ✖ Planned or expected spinal fixation surgery during the study period (as judged by the Investigator, i.e. due to rapidly progressing scoliosis), prior spinal fixation surgery is allowed if it took place more than 6 months prior to Screening.
- ✖ Asthma, bronchitis/COPD, bronchiectasis, emphysema, pneumonia or presence of any other non-DMD respiratory illness that affects respiratory function.
- ✖ Chronic use of beta2-agonists or any use of other bronchodilating/bronchoconstricting medication (inhaled steroids, sympathomimetics, anti-cholinergics and antihistamines); chronic use is defined as a daily intake for more than 14 days.
- ✖ Any bronchopulmonary illness that required treatment with antibiotics within 3 months prior to Screening.
- ✖ Moderate or severe hepatic impairment (use as guidance Child-Pugh class B [7 to 9 points or Child-Pugh class C [10 to 15 points] or severe renal impairment (eGFR <30 mL/min/1.73 m2).
- ✖ Prior or ongoing medical condition or laboratory abnormality which in the Investigator's opinion may put the patient at significant risk, may confound the study results or may interfere significantly with the patient's participation in the study (please see below Note).
- ✖ History of or current drug or alcohol abuse or use of any tobacco/marijuana products/smoking.
- ✖ Known individual hypersensitivity to idebenone or to any of the ingredients/excipients of the study medication.
- ✖ Daytime ventilator assistance (defined as use of any assisted ventilation while awake).

Note: Patients who suffer from a severe, unstable condition including (but not limited to) cancer, auto-immune diseases, hematological diseases, metabolic disorders or immunodeficiencies, and who are at risk of an aggravation unrelated to the study condition, can only be included in the study if accepted in writing by the Sponsor's Senior Clinical Research Physician.

For contact details and to find out more, please refer to dmdhub.org.

Duchenne UK