At Santhera, we’re studying a potential new treatment option to slow the progression of respiratory function decline in Duchenne.
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Educational Purposes

The following presentation is for educational purposes. It features information about:

• Duchenne muscular dystrophy
• Understanding the importance of respiratory health in Duchenne
• Santhera’s role in studying a potential treatment option
• Potential participation in Duchenne clinical trials

This presentation is intended for educational purposes only. It is intended for informational purposes only, and should not be used in place of a discussion with a health care professional. All decisions regarding patient care must be handled by a health care professional, and be made based on the unique needs of each patient.
Meet Santhera

US headquarters in Burlington, MA with global headquarters in Pratteln, Switzerland

Working to develop idebenone for Duchenne since 2008

3 completed studies and 1 ongoing study in Duchenne; majority of clinical trial patients were non-ambulatory

Approved for Leber’s Hereditary Optic Neuropathy (LHON) in Europe

OUR PIPELINE

- idebenone in DMD (Duchenne muscular dystrophy) - Phase 3
- omigapil in CMD (Congenital muscular dystrophy) - Phase 1
- POL6014 in CF (Cystic Fibrosis) - Phase 1
Duchenne and Respiratory Health

In Duchenne, the muscles that support breathing weaken in the same way that leg and heart muscles weaken.

**Over time, little-by-little, the respiratory system loses strength which means:**

- Supporting muscles continue to weaken
  - This can make the lungs less effective at moving air in and out
- Cough gets weaker
- Changes that seem minor or go unnoticed can become more serious complications

Respiratory complications are one of the leading causes of death in Duchenne.
How to Protect Respiratory Health: Good Care and Be Aware

Protecting respiratory health means being mindful of small changes through regular testing and symptom management.

GOOD CARE

• Have a care team of experts starting with a neurologist
• See pulmonologist every year, 2 times/year if non-ambulatory
  o While still able to walk, boys should have a respiratory test
  o Lung function tests can help signal if there is trouble breathing now or in the future

BE AWARE

• Watch symptoms closely when non-ambulatory for early signs that respiratory muscles are weakening:
  o Headaches
  o Restless sleep
  o Shallow breathing at night
  o Trouble concentrating
  o Difficulty staying awake
  o Unexpected weight loss

• Protect against infections and clear airways on a regular basis
  o Get flu and pneumococcal vaccines
  o Watch colds carefully
Welcome to TakeabreathDMD.com

As a proud partner of the Duchenne community, we’re happy to introduce TakeabreathDMD.com

You'll find valuable information about DMD respiratory health including:

• Ways to help manage lung function and well-being
• How to address respiratory complications
• Helpful news about DMD when you sign up for updates

Take a look for yourself and see what TakeabreathDMD.com has to offer.
What Is Idebenone?

Idebenone is an investigational oral tablet that works within the mitochondria.
Idebenone in Duchenne Clinical Trials

DELOS: Phase 3 trial in patients in respiratory decline not using steroids (complete)

**Objective:** to study the efficacy of idebenone compared to placebo, on respiratory function in patients with Duchenne not using steroids.

**Study design and patients**

- **64** males with Duchenne
- **92%** of patients were non-ambulatory
- **17** centers around the world
- **52** weeks

Idebenone or placebo
DELOS Primary Endpoint: The primary endpoint was a change from baseline to week 52 in PEF%p (percent predicted peak expiratory flow)
  • PEF measures peak or maximum flow of air when a boy breathes out as hard as he can

DELOS PEF Outcome: The decline in PEF%p from baseline to week 52 was 3.05% for the idebenone group versus 9.01% for the placebo group (p=0.044)
  • There was a 66% reduction in loss of PEF%p between the treatment group and the placebo group

DELOS Side Effects: The most common side effects were diarrhea, abdominal pain, nasopharyngitis (common cold), and headache. Overall treatment was well-tolerated.
**Objective:** to study the efficacy of idebenone compared to placebo, in delaying the loss of respiratory function in patients with Duchenne who are using steroids.

**SIDEROS:** Phase 3 trial in patients using steroids (ongoing)

**Study design and patients**

- **266** males with Duchenne
- **10** years of age and older who are using steroids
- **64** centers worldwide (23 in the US)
- **78** weeks

- Idebenone or placebo
Idebenone in Duchenne Clinical Trials (SIDEROS)

Inclusion Criteria:

- Independent of dystrophin mutation type
- Boys and men with a forced vital capacity (FVC) between 35% and 80% of predicted value
- Any regimen of prednisone (prednisolone) or deflazacort (calcort)
- Corticosteroids use for at least 12 months prior to randomization without any dose adjustments in last 6 months

Exclusion Criteria:

- Those needing daytime ventilation assistance
- Cannot be part of any other ongoing therapeutic trial or any experimental drug within 90 days prior to start of SIDEROS participation

*The total amount forcibly blown out after one big breath. FVC scores indicate the degree to which the lungs are inflating to full capacity.*
SIDEROS Clinical Trial Sites

Visit [www.Siderosdmd.com](http://www.Siderosdmd.com) for an in-depth trial overview

ClinicalTrials.gov identifier: NCT#02814019

Jodi Wolff, PhD
Jodi.wolff@santhera.com
Sideros@santhera.com
Santhera is a proud partner of the Duchenne community.
Thank you for joining us today.

At Santhera, we believe information and support can be empowering.
Welcome to BreatheDMD.com

BreatheDMD is an expanded access program that may allow eligible patients with DMD to gain access to idebenone.

Visit www.breathedmd.com for more information.
SIDEROS – US Clinical Trial Sites

Dr. Bradley Troxler
University of Alabama
Birmingham, Alabama

Dr. James Woodward
Phoenix Children’s Hospital
Phoenix, Arizona

Dr. Cori Daines
Banner–University Medical Center
Tucson, Arizona

Dr. Vikki Stefans
Arkansas Children’s Hospital
Little Rock, Arkansas

Dr. David Michelson
Loma Linda University Medical Center
Loma Linda, California

Dr. Leigh Maria Ramos-Platt
Children’s Hospital of Los Angeles
Los Angeles, California

Dr. Perry Shieh
David Geffen School of Medicine at UCLA
Los Angeles, California

Dr. Craig McDonald
UC Davis Department of Physical Medicine and Rehabilitation
Sacramento, California

Dr. Marisa Couluris
Shriners Hospitals for Children
Tampa, Florida

Dr. Han Phan
Center for Integrative Rare Disease Research
Atlanta, Georgia

Dr. Kathy Mathews
University of Iowa
Iowa City, Iowa

Dr. Jeffrey Statland
University of Kansas Medical Center
Kansas City, Kansas

Dr. Thomas Crawford
Johns Hopkins University Hospital
Baltimore, Maryland

Dr. Basil Darras
Boston Children’s Hospital
Boston, Massachusetts

Dr. Stephen Smith
Gillette Children’s Specialty Healthcare
St Paul, Minnesota

Dr. Emma Ciafaloni
University of Rochester
Rochester, New York

Dr. Benjamin Brooks
Carolinas HealthCare System
Charlotte, North Carolina

Dr. Cuixia Tian
Cincinnati Children's Hospital Medical Center
Cincinnati, Ohio

Dr. Andre Prochoroff
MetroHealth Medical Center
Cleveland, Ohio

Dr. Oscar Henry Mayer
Children’s Hospital of Philadelphia
Philadelphia, Pennsylvania

Dr. Tulio Bertorini
Wesley Neurology Clinic
Memphis, Tennessee

Dr. Warren Marks
Cook Children’s Medical Center
Fort Worth, Texas

Dr. Russell Butterfield
University of Utah School of Medicine
Salt Lake City, Utah