Friedreich Ataxia: Disease Overview and Management Options

A Resource for Clinicians

Background

- Friedreich Ataxia (FRDA, often referred to as FA) is a rare, genetic, autosomal recessive disease and the most common form of hereditary ataxia
- FRDA is optimally managed by a multidisciplinary team. Prior to 2023, no therapies were available. Omaveloxolone was FDA-approved to treat FRDA in patients ≥16 years of age (February 2023).
- Information in this document highlights key points from an MDA-hosted mini-webinar with a neurologist with extensive experience managing FRDA. **View the companion mini-webinar here.**

Overview[1-5]

Description

- Progressive neurodegenerative movement disorder that results in gait and limb ataxia
- Caused by mutation in the frataxin (*FXN*) gene, which encodes frataxin protein

Epidemiology

- Prevalence of ~1 in every 50,000 people in the United States
- More prevalent in European ancestry
- Affects males and females equally
- Estimated 5000 patients in the United States

Onset

- Typical FRDA manifests between 5 and 15 years of age for 75% of patients
- Late onset FRDA* develops after 25 years of age

Prognosis

- Varies depending on severity of symptoms and is often correlated with age of onset
  - Severe with earlier onset
- Wheelchair bound 10 to 20 years after initial symptoms
- Life expectancy is shortened

*Includes late-onset (>25 years of age), very late-onset (>40 years of age), and FRDA with retained reflexes in the tendons.

1. Cook A, Giunti P. Br Med Bull. 2017;124(1):19-30. 2. Lynch DR, et al. J Multidiscip Healthc. 2021;14:1645-1658. 3. National Institute of Neurological Disorders and Stroke. Friedreich ataxia. https://www.ninds.nih.gov/health-information/disorders/friedreich-ataxia. 4. Corben LA, et al. Orphanet J Rare Dis. 2022;17(1):415. 5. Bidichandani SI, Delatycki MB. Friedreich ataxia. In: Adam MP, et al., eds. GeneReviews®. Seattle, WA; December 18, 1998 [updated 2017].

Pathology Associated with FXN Mutation[1-3]

Degeneration of three major neurological systems

- Large fiber sensory systems
- Cerebellar coordination
- Corticospinal motor systems

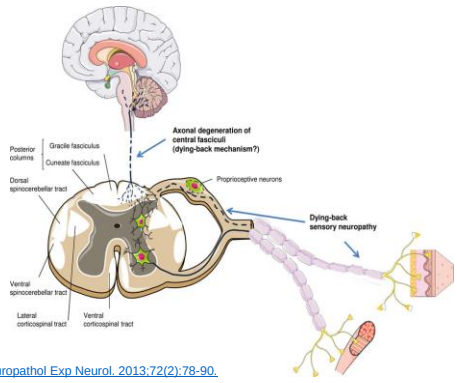

Figure used with permission from González-Cabo P. J Neurochem. 2013;126 Suppl 1:53-64.

1. Lynch DR, et al. J Multidiscip Healthc. 2021;14:1645-1658. 2. Cook A, Giunti P. Br Med Bull. 2017;124(1):19-30. 3. Koeppen AH, Mazurkiewicz JE. J Neuropathol Exp Neurol. 2013;72(2):78-90.

Genetic testing is a cornerstone of diagnosis.
With the appropriate test, diagnosis can be confirmed in nearly all patients with FRDA.

Developed with the expertise of David Lynch, MD, PhD, Children's Hospital of Philadelphia
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Clinical Features[1-4]

Neurological abnormalities

- Progressive gait and limb ataxia
- Babinski sign
- Loss of balance and vibration
- Impaired proprioception
- Dysmetria
- Hearing loss
- Loss of deep tendon reflexes
- Dysarthria
- Oculomotor abnormalities
- Vision loss
- Dysphagia

Cardiac conditions

- Cardiac dysfunction
  - Leading to premature mortality
- Cardiomyopathy
  - Heart failure
  - Arrhythmias

Orthopedic conditions

- Scoliosis (60% of patients)
- Reduced bone mineral density

Other

- Diabetes mellitus
- Urinary frequency/urgency
- Slightly decreased height and BMI
- Sleep-disordered breathing

A Variable Clinical Phenotype: Management Requires Multidisciplinary Care[1-3]

Rehabilitation/Holistic Care

- Physical therapy
- Occupational therapy
- Speech/language therapy

Specialist Care

- Cardiology
- Neurology
- Orthopedics
- Ophthalmology
- Urology
- Sleep physician

Monitoring

- Neurological
- Musculoskeletal
- Cardiac (clinical, ECG, echo)
- Endocrine (HbA1c)
- Visual screening
- Auditory assessments

1. Lynch DR, et al. J Multidiscip Healthc. 2021;14:1645-1658. 2. Cook A, Giunti P. Br Med Bull. 2017;124(1):19-30. 3. Koeppen AH, Mazurkiewicz JE. J Neuropathol Exp Neurol. 2013;72(2):78-90. 4. Bidichandani SI, Delatycki MB. Friedreich ataxia. In: Adam MP, et al., eds. GeneReviews®. Seattle, WA; December 18, 1998 [updated 2017].

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Therapeutic Options: Omaveloxolone (approved 2023)[1-2]

FDA-approval based on:

1. **MOXIe Part 2 clinical study (NCT02255435)**
2. **MOXIe Extension: Delayed start analysis and propensity matched analysis**

- Indicated for FRDA in individuals aged ≥16 years

FDA, Food and Drug Administration; FRDA, Friedreich ataxia
1. Skyclarys [prescribing information]. Plano, TX: Reata Pharmaceuticals, Inc.; 2023. 2. Lynch DR, et al. Movement Disorders. 2023;38(2):313-320.

Ongoing Clinical Research (as of April 2023)*

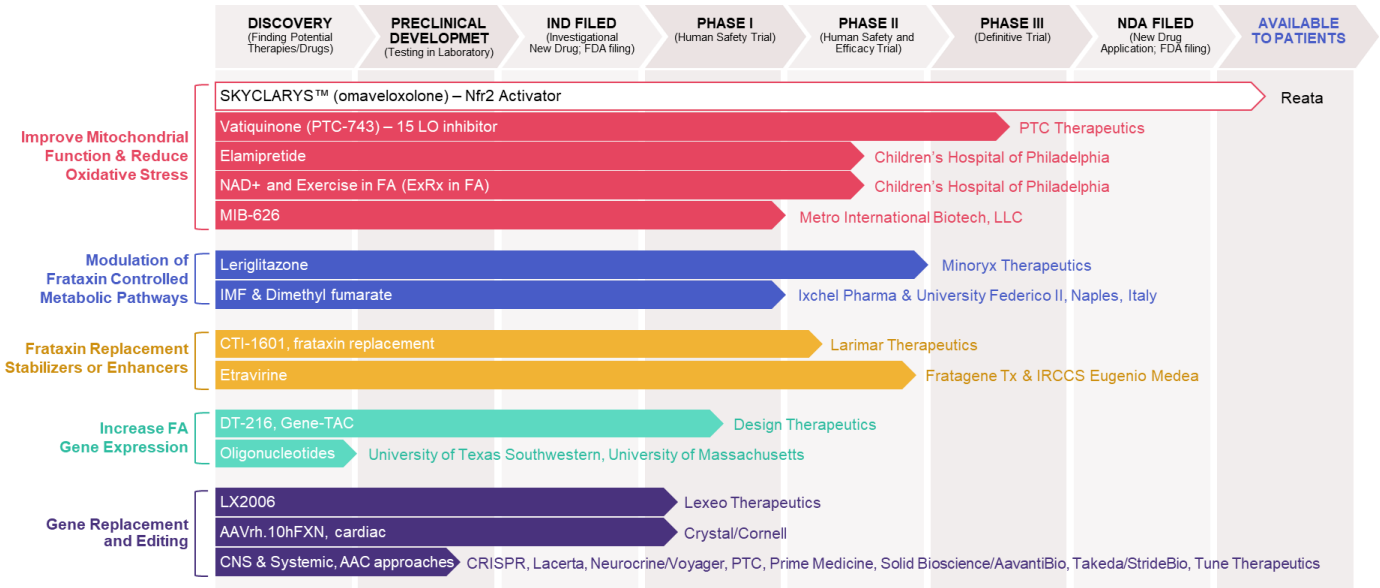

*Figure courtesy of Friedrich's Ataxia Research Alliance (FARA). Used with permission (personal communication). © 2023 FARA.
To access the most up-to-date version, view online at https://www.curefa.org/research/research-pipeline

Additional Resources: FRDA Management

FRDA Management Guidelines (2022)


Orphanet Journal of Rare Diseases

POSITION STATEMENT — Open Access

Clinical management guidelines for Friedreich ataxia: best practice in rare diseases

Louise A. Corben, Veronica Collins, Sarah Milne, Jennifer Farmer, Ann Musheno, David Lynch, Sub Subramony, Massimo Pandolfo, Jörg B. Schulz, Kim Lin and Martin B. Delatycki, on behalf of the Clinical Management Guidelines Writing Group

Abstract

Omaveloxone: Navigating Access (REACH)

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