



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

A double-blind, randomized, placebo-controlled trial to test the efficacy, safety and tolerability of Dimethyl Fumarate in Friedreich Ataxia (DMF-FA-201).

2022-503016-16-00

Trial status	
Application status:	
Authorised	
Overall trial status:	
Authorised	

Trial identifiers	
Clinical trial identifiers	
<p>EU trial number:</p> <p>2022-503016-16-00</p> <p>Full title (English):</p> <p>A double-blind, randomized, placebo-controlled trial to test the efficacy, safety and tolerability of Dimethyl Fumarate in Friedreich Ataxia (DMF-FA-201).</p> <p>Public title (English):</p> <p>A double-blind, randomized, placebo-controlled trial to test the efficacy, safety and tolerability of Dimethyl Fumarate in Friedreich Ataxia (DMF-FA-201).</p> <p>Protocol code:</p> <p>DMF-FA-201</p>	
Secondary identifying numbers	
<p>WHO universal trial number (UTN):</p> <p>ClinicalTrials.gov identifier (NCT number):</p> <p>ISRCTN number:</p>	
Additional registries	
<p>Registry name:</p> <p>EudraCT</p> <p>Registry identifier:</p> <p>2021-006274-23</p>	

Trial Information	
Transition Trial	
EudraCT number:	
Trial category	
<div>Low Intervention clinical trial:</div> <div>No</div> <div>Justification of the low interventional clinical trial:</div> <div>Trial phase:</div> <div>Therapeutic exploratory (Phase II)</div> <div>Trial Category:</div> <div>Category 2</div> <div>Justification for trial category:</div> <div>No profit Phase II Clinical Trial</div>	
Main objective	
<div>Trial scope:</div> <div>Efficacy, Other, Safety</div> <div>Main objective (English):</div> <div>To test the effect of DMF on FXN transcription and frataxin protein in FRDA patients.</div>	
Secondary objective	
<div>Secondary Objective Number:</div> <div>1</div> <div>Secondary objective (English):</div> <div>To test the effect of DMF on the nrf2 pathway, on mitochondrial biogenesis, safety and tolerability, and clinical aspects of the disease.</div>	

Primary end points
<div>End points:</div> <div><div><div>End Point Criteria Number:</div><div>1</div><div>Primary end point (English):</div><div>The effect of DMF compared to placebo on one of two co-primary endpoints (achievement of one out of two is a positive result): FXN gene expression and frataxin protein level. For both we will consider the change from baseline to 12 weeks (core phase of the DMF-FA-201 study).</div></div></div>
Secondary end points
<div>End points:</div> <div><div><div>Secondary End Point Number:</div><div>1</div><div>Secondary end point (English):</div><div>Effect of DMF on the cardiopulmonary exercise outputs (VO2max, anaerobic threshold, peak workload)</div></div><div><div>Secondary End Point Number:</div><div>2</div><div>Secondary end point (English):</div><div>Effect of DMF on echocardiographic measures</div></div><div><div>Secondary End Point Number:</div><div>3</div><div>Secondary end point (English):</div><div>Effect of DMF on FXN and frataxin protein from pooled data from the core and extension phase of the study</div></div><div><div>Secondary End Point Number:</div><div>4</div><div>Secondary end point (English):</div><div>Effect of DMF on FXN and frataxin protein at week 4 of the core phase</div></div></div>

<p>Secondary End Point Number:</p> <p>5</p> <p>Secondary end point (English):</p> <p>Effect of DMF on Nrf2 pathway genes: NFE2L2, NQO1, HMOX1, PDLIM1, NCF2</p>
<p>Secondary End Point Number:</p> <p>6</p> <p>Secondary end point (English):</p> <p>Effect of DMF on mitochondrial biogenesis genes (mt-ND6, mtCYB, mt-CO2, mt-ATP6) and on mtDNA/nDNA</p>
<p>Secondary End Point Number:</p> <p>7</p> <p>Secondary end point (English):</p> <p>Number and distribution of serious and non-serious adverse events between DMF and placebo</p>
<p>Secondary End Point Number:</p> <p>8</p> <p>Secondary end point (English):</p> <p>Difference in the Scale for the Rating and assessment of Ataxia (SARA) and modified Friedreich Ataxia Rating Scale (mFARS) between DMF and placebo</p>
<p>Secondary End Point Number:</p> <p>9</p> <p>Secondary end point (English):</p> <p>Difference in the 9-hole pegboard test (9HPT) between DMF and placebo</p>
<p>Secondary End Point Number:</p> <p>10</p> <p>Secondary end point (English):</p> <p>Difference in the EQ-5D and ADL/IADL between DMF and placebo</p>
Medical Conditions

Medical condition(s) (English):

Friedreich's Ataxia

Is the medical condition considered to be a rare disease:

No

Medical condition(s) MedDRA information
<div><div>Version:</div><div>20.0</div><div>Level:</div><div>PT</div><div>Classification Code:</div><div>10017374</div><div>Term Name:</div><div>Friedreich's ataxia</div><div>System Organ Class:</div><div>100000004850</div></div>
Trial duration
<div><div>Estimated start date:</div><div>01/06/2023</div><div>Estimated global end of trial date:</div><div></div><div>Estimated end of trial date in EEA:</div><div>01/06/2024</div></div>
Source of monetary or financial support
<div><div>Organisation Name:</div><div>AIFA, ALMIRALL S.A.</div></div>
Individual Participant Data (IPD) Sharing statement

Plan To Share IPD:

Plan Description:

Principal inclusion criteria

Criteria:

Inclusion Criteria Number:

1

Principal inclusion criteria (English):

Molecular diagnosis of Friedreich Ataxia with a homozygous GAA expansion

Inclusion Criteria Number:

2

Principal inclusion criteria (English):

Age ≥12 years

Inclusion Criteria Number:

3

Principal inclusion criteria (English):

Body weight ≥30 Kg

Inclusion Criteria Number:

4

Principal inclusion criteria (English):

Patients able to read and sign the informed consent

Principal exclusion criteria**Criteria:****Exclusion Criteria Number:**

1

Principal exclusion criteria (English):

Treatment with DMF in the previous 12 months

Exclusion Criteria Number:

10

Principal exclusion criteria (English):

Positive history of alcohol or drug abuse in the past 2 years, except for medical use of cannabis

Exclusion Criteria Number:

11

Principal exclusion criteria (English):

Hypersensitivity to DMF or any other component of the study drug

Exclusion Criteria Number:

12

Principal exclusion criteria (English):

Patients not able to comply with the study

Exclusion Criteria Number:

13

Principal exclusion criteria (English):

For female patients (Sexually not active, hysterectomized, sterilized, menopause patients are excluded from the following criteria): - Pregnancy, or - Breastfeeding, or - Inadequate contraception

Exclusion Criteria Number:

2

Principal exclusion criteria (English):

Treatment with Idebenone, coenzyme Q10, or any other vitamin supplements in the previous 30 days

Exclusion Criteria Number:

3

Principal exclusion criteria (English):

Patients in treatment with any other not allowed drug

Exclusion Criteria Number:

4

Principal exclusion criteria (English):

Any Cardiac and/or Renal and/or Hepatic disease judged as clinically significant by the investigator (any abnormal and clinically non significant cardiac disease associated with Friedreich Ataxia is not an exclusion criteria)

Exclusion Criteria Number:

5

Principal exclusion criteria (English):

Any clinically significant ECG abnormalities that may interfere with the study

Exclusion Criteria Number: 6 Principal exclusion criteria (English): Any abnormal and clinically significant laboratory exams at screening visit that may interfere with the trial	
Exclusion Criteria Number: 7 Principal exclusion criteria (English): Any acute disease that could interfere with the study, as judged by the investigator	
Exclusion Criteria Number: 8 Principal exclusion criteria (English): Patient positive to the Human Immunodeficiency Virus (HIV) or Hepatitis B or C test	
Exclusion Criteria Number: 9 Principal exclusion criteria (English): Patients with a positive history of neoplasia, with the only exception of a completely excided basal cell carcinoma	

Population of trial subjects
<p>Gender:</p> <p>Male and Female</p> <p>Age range:</p> <p>0-17 years, 18-64 years, 65+ years</p> <p>Age range secondary identifier:</p> <p>12-17 years, 18-64 years</p> <p>Clinical trial group:</p> <p>Patients</p> <p>Recruitment population groups:</p> <p>Women of child bearing potential using contraception</p> <p>Emergency situation description:</p>

Protocol information	
Study design	
<div><div>Period Details:</div><div></div></div> <div><div>Roles blinded:</div><div></div></div> <div><div>Term name:</div><div>Friedreich's ataxia</div></div> <div><div>Level:</div><div>PT</div></div> <div><div>Classification code:</div><div>10017374</div></div> <div><div>Version:</div><div>20.0</div></div>	

Study design
Arm details:

Scientific advice and paediatric investigation plan (PIP)	
Competent authorities that have provided scientific advice:	
EMA paediatric investigation number:	
Associated clinical trials	
References	
Reference to publication:	
Reference link to publication:	

Role: Test Name: Skilarence 120 mg gastro-resistant tablets

Product: PRD5131533, PRD5140716, PRD5140785, PRD5140931	
Medicinal product details	
EU Medicinal Product number/medicinal product unique ID: PRD5131533, PRD5140716, PRD5140785, PRD5140931	
Is this a specific paediatric formulation: No	
Strength: Dimethyl Fumarate 120mg	
Medicinal product name: Skilarence 120 mg gastro-resistant tablets	
Product authorisation status: Authorised	
Pharmaceutical Form: GASTRO-RESISTANT TABLET	
Medicinal product other name:	
Sponsors product code:	
Medicinal product role in trial: Test	
Other medicinal product:	
Products characteristics	

Dosage and Administration Details**Route of administration:**

ORAL

Maximum duration of treatment:

24.0 Week(s)

Maximum daily dose allowed:

480

Daily dose unit of measure:

mg milligram(s)

Maximum total dose allowed:

480

Total dose unit of measure:

mg milligram(s)

Information about the modification of the medicinal product**Has the medicinal product been modified in relation to its Marketing Authorisation:**

No

Description of the modification:**Product classification****Anatomical Therapeutic Chemical (ATC) Codes:**

L04AX07

ATC name:

-

ATC level:

5

Product authorisation details

<div><div>Marketing authorisation number:</div><div>EU/1/17/1201/004</div><div>Marketing Authorisation Country:</div><div>EU</div><div>Centralised procedure/MRP/DCP/registration procedure number:</div><div>EMA/H/C/002157</div><div>Marketing authorisation holder:</div><div>ALMIRALL, S.A.</div></div>
Orphan designation
<div><div>Does this product have an orphan drug designation:</div><div>No</div><div>Designation number for orphan drug:</div></div>
Active substance
<div><div>Active Substances:</div><div>DIMETHYL FUMARATE</div><div>Active Substance other descriptive name:</div><div>Sponsor substance Code:</div></div>

Active Substance name:

DIMETHYL FUMARATE

Strength:

120mg

EU Active Substance Code:

SUB13608MIG

Active substance other descriptive name:

Classification:

Chemical

Status:

Approved

Active substance name synonyms:

BG00012, FP 187

Is this product an Advanced Therapy Medicinal Product (ATMP)?

No

Advanced therapy medicinal product

Device associated with medicinal product

Compliance with (gmp) for the medicinal product

Authorisation number of manufacturing and import:

Authorisation number of manufacturing and import:

IMPD quality
Justification for no IMPD upload:
IMPD - safety and efficacy
Justification for no IMPD upload:

Role: Placebo Name: Placebo of Dimethyl fumarate 120 mg gastro-resistant tablets

Compliance with (gmp) for the medicinal product

Authorisation number of manufacturing and import:

Authorisation number of manufacturing and import:

Manually added Placebos – Description of the placebo

Placebo of Dimethyl fumarate 120 mg gastro-resistant tablets

Linked Products:

Sponsor: Dipartimento Di Neuroscienze E Scienze Riproduttive Ed Odontostomatologiche Universita
Degli Studi Di Napoli Federico II

Sponsor details

Name of sponsor organisation:

Sponsor type:

Country:
Italy

Town/ City:

Post Code:

Address - Street name:

Telephone number:

Email address:

Sponsor: Dipartimento Di Neuroscienze E Scienze Riproduttive Ed Odontostomatologiche Universita Degli Studi Di Napoli Federico II
Legal representative

Name of Legal Rep Organisation:

Sponsor(s) Legal Representative:

Address:

Post Code:

Town / City:

Country:

Organisation email address:

Contact person - First name:

Contact person - Last name:

Telephone number:

Clinical trial person email address:

Sponsor: Dipartimento Di Neuroscienze E Scienze Riproduttive Ed Odontostomatologiche Universita Degli Studi Di Napoli Federico II

Scientific contact point

Name of organisation:

Dipartimento Di Neuroscienze E Scienze Riproduttive Ed Odontostomatologiche Universita Degli Studi Di Napoli Federico II

Telephone number:

+393470734774

Functional contact point name:

Francesco Saccà

Email address:

francesco.sacca@unina.it

Public contact point

Name of organisation:

Dipartimento Di Neuroscienze E Scienze Riproduttive Ed Odontostomatologiche Universita Degli Studi Di Napoli Federico II

Telephone number:

+393470734774

Functional contact point name:

Francesco Saccà

Email address:

francesco.sacca@unina.it

3rd party associated with the trial

Responsibilities of the sponsor

No responsibility has been yet assigned to the sponsor

Summary	
Trial status:	
Authorised	
Submission date:	
29/12/2022	