FA Integrated Clinical Database (FA-ICD) via RDCA-DAP

This initiative represents a collaborative partnership between the Friedreich's Ataxia Research Alliance (FARA) and the Rare Diseases Cures Accelerator Data and Analytic platform (RDCA-DAP) of the Critical Path Institute (C-Path), with a goal of making Friedreich's ataxia clinical research and trial data available to the research community through a secure platform.

The Rare Disease Cures Accelerator-Data and Analytics Platform (RDCA-DAP®) is an FDA-funded initiative that provides a centralized and standardized infrastructure to support and accelerate rare disease characterization, with the goal of accelerating therapy development across rare diseases. This platform is made possible through a collaborative grant from the FDA [Critical Path Public-Private Partnerships Grant Number U18 FD005320 from the U.S. Food and Drug Administration].

RDCA-DAP houses integrated patient-level data from diverse sources, including clinical trials, longitudinal observational studies, patient registries, and real-world data (e.g. electronic health records) across a multitude of rare diseases. Data are contributed from different organizations and companies around the world. These data are curated and standardized from FA clinical trials and natural history studies into CDISC format. The data are available to qualified researchers who may access and analyze data in aggregate, or filter and view individual de-identified patient-level data.

FA Data available in RDCA-DAP include:

Dataset	Number of Patients	Frequency of Follow up	Duration of Study	Variables Collected
FA-COMS	810	Baseline, yearly	13 years	FARS, 9-hole peg test, 25 foot walk , visual acuity, functional staging for ataxia, quality of life and activities of daily living scales, Demographics, and event- based outcomes.
Santhera –Ionia	35 (70 at baseline)	Baseline, week 4, week 12, week 24	24 weeks	FARS, ICARS, 9 hole peg test, 25 foot walk, demographics
Santhera – Miconos	131 (232 at baseline)	Screening, baseline, week 24 and week 52	1 year	FARS, ICARS, demographics
Apopharma – deferiprone	17	Screening, baseline	Baseline	FARS, ICARS, 9 hole peg test, 25 foot walk, activities of daily living and quality of life scales, ECG, labs, visual acuity, vitals
Bioelectron – EPI-743	21	Screening, Baseline, Month 1, Month 3, Month 6	6 months	FARS, 9 hole peg test, visual acuity GAA repeat 1 and 2, reason withdraw from study, PGI, activity of daily living scale
Horizon	92	Baseline, 3 months, 6 months	6 months	FARS, medications, ECG, labs, ADL, PEDSQL, SF-36, demographics, vital signs
Takeda*	87	Screening, Baseline, 2 weeks, 6 weeks, 2 months	2 months	FARS, ADL, medications, ECG, eye data, lab, CGI, PGI, C-SSRS, vital signs

Dataset	Number of Patients	Frequency of Follow up	Duration of Study	Variables Collected
EFACTS*	607	Baseline, yearly	4.6 years	SARA, 9-hole peg test, 8-meter (25 foot) walk, ADL, GAA, ECG, Demographics, Medical history, Physical exam, EQ5D, INAS
FA-CHILD**	108	Baseline, 6 months	3 years	FARS, BBS, 9-hole peg test, TUG, ADL, 25-foot walk, 6-minute walk, Frataxin gene info, PEDSQL, vital signs, demographics, medical history, FA symptoms, medications
EHR Synthetic data (Replica)	X	X	X	X

RDCA-DAP Portal has detailed instructions for application to the platform and accessing data sets and workspaces - https://portal.rdca.c-path.org/

Data Contributions
We encourage data contributions from interventional and non-interventional studies and are always willing to discuss how companies or other researchers can engage with the initiative. For more information on RDCA-DAP, the FA data sets and/or how your organization can contribute data, please contact Alexandre Betourne, abetourne@c-path.org or rdcadap@c-path.org.

Important information about FA-ICD content and access:

- The data platform contains, but is not limited to:
    - Demographic data
    - Friedreich's Ataxia Rating Scale (FARS)
    - International Co-operative Ataxia Rating Scale (ICARS)
    - Activities of Daily Living Scale
    - Functional Disability Scale
    - 25-Foot Walk
    - 9-Hole Peg Test
    - Modified Fatigue Impact Scale (MFIS)
    - MOS Pain Effects Scale (PES)
    - Bladder Control Scale (BLCS)
    - Bowel Control Scale (BWCS)
    - Impact of Visual Impairment Scale (IVIS)
    - Sloane low contrast letter acuity scale. (LCLA)
    - SF-10 and SF-36
    - Vital signs
    - ECG
    - Echocardiogram
    - Genetic mutation
- C-Path has fully anonymized all data.
- Researchers must agree to the Terms and Conditions for Use of the FA-ICD data platform and submit an online application form to request access to the data platform.
- The FA-ICD Steering Committee approves data access for external users.
- The Resources tab within FA-ICD contains information to help users understand and make use of the platform capabilities.

Important information about data standardization:

- C-Path has normalized all data to the CDISC Study Data Tabulation Model (CDISC SDTM) to enable researchers to analyze the data in aggregate.
- FA-ICD provides basic information on how data are structured using CDISC. Knowledge of SDTM is required for effective use of the data. Information and

training about SDTM are available through the CDISC website; researchers who receive access to FA-ICD will find a link to the CDISC website on the Resources tab.

A summary of detailed concepts captured by SDTM domains contained in the FA-ICD is provided in the table below.

CDISC Domain	Contents
CE	Clinical events
CM	Medications
CV	LVEF, LVSF, LVMass, LVIDD, LVIDS, IVS, ejection fraction, fractional shortening, valve regurgitation, wall motion, wall thickness, LVOT, LVIT, interpretation
DD	Age at death, autopsy indicator, death certificate obtained, hospital medical record obtained, cause of death
DM	Age, gender, race, ethnicity, trial arm, country
DS	Withdrawal, death, lost to follow up, reconsent
DU	Assistive walk device indicator, type, age
EG	Mean heart rate, PR, QRS duration, QT, QTc, interpretation
FA	Occurrence and completion indicators, reason for missing visit
FT	FARS*, 25-Foot Walk, 9-Hole Peg Test, Functional Staging for Ataxia
LB	ALT, AST, creatinine, corrected leukocytes, ferritin, glucose, hemoglobin, neutrophils, neutrophils/leukocytes, platelets, nucleated erythrocytes/leukocytes, leukocytes, zinc
MH	Medical history events
OE	Letter eye chart, cataract surgery laterality, require correction for vision indicator
PE	Physical exam
PR	Scoliosis surgery, cardiac procedures
QS	Activities of Daily Living, SF-10, SF-36, PGI, BLCS, BWCS, MFIS, IVIS, PedsQL, PES
RE	FEV1, FEV1/FVC, FVC, FEF25-75, percent predicted, indication, interpretation
RP	Pregnancy confirmed, birth control method, pregnancy outcomes
RS	International Co-operative Ataxia Rating Scale (ICARS)*
SC	Level of education, living status, marital status, occupation
SS	Change in ambulation status
VS	Height, weight, BMI, pulse rate, DBP, SBP, heart rate

* Note: The FARS is located in the FT domain because the answers to the questions are governed by the duration/number of times a patient could perform the task. The ICARS is located in the RS domain because the answers are more subjectively answered by the

clinician/technician who is observing the patient performing the task.