THE FA GCC GLOBAL CLINICAL CONSORTIUM

Background

There are two well-established, long-standing natural history studies in Friedreich ataxia (FA) that have significantly contributed to our understanding of how FA affects individuals and provided a framework for further investigation of clinical measures that can quantitatively assess disease progression.

FACOMS (US, Canada, Australia, New Zealand and India)
EFACTS (European Union Countries)

These studies have been conducted in parallel with many similarities in protocol design, objectives and study conduct. The investigators of both FACOMS and EFACTS see the need to combine efforts into a single global consortium with a unified natural history and clinical research infrastructure.

The new FA Global Clinical Consortium and a harmonized global study protocol, The UNIFAI Study, have been established to continue to improve the panel of outcome measures that can be used in FA clinical trials, to better organize and harmonize the natural history ecosystem and allow for a more complete view of disease progression of FA.

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The consortium participation includes investigators from 33 clinical sites representing 18 countries.

Figure 1: The FA GCC includes 33 sites representing 18 countries

Mission & Membership

***FA GCC Mission Statement*:** Accelerate the development of treatments for Friedreich Ataxia by empowering patients and researchers, understanding natural history, conducting research and developing infrastructure that facilitates clinical research across the globe.

The FA GCC was established to provide:

- A more complete view of the natural history of FA through a larger global patient cohort and the highest quality dataset
- International standards for assessments and align on recommenations to biopharma companies and regulatory bodies
- A platform for broad collaboration between researchers, empowering the FA academic and clinical community

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Organizational Structure

The FA GCC virtual consortium has built a collaborative network leveraging existing resources and staff. The structure and communication encourages balanced global interaction and partnership.

The consortium structure is comprised of a funding board, scientific steering committee, management team, work groups, patient advocacy team and the Investigator members of each clinical site (Figure 2).

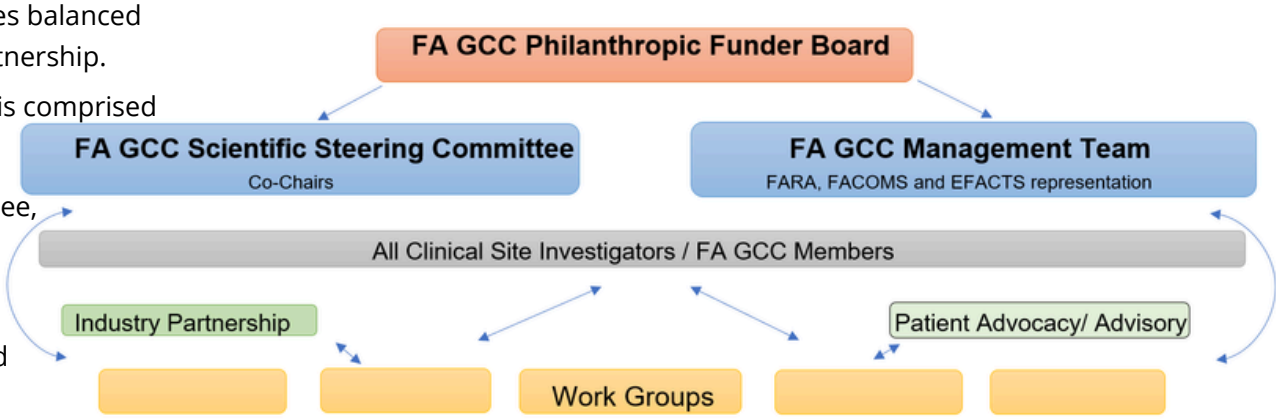

Figure 2: Consortium Structure

Site Survey

How far does the average patient travel to come to your site?

250 KILOMETERS [20-800 KM]

What percentage of your patients require reimbursement for travel that would include airfare and hotel?

43% [0-100%]

What portion of your site's patient population also receive clinical care during an annual natural history visit?

73% [0-100%]

As one of the first undertakings, a survey was distributed to both active and interested member sites to collect important information about each site.

Goals of this site survey included collecting:

- General site information
- Current/future volume of FA patients
- Capabilities for industry studies [CTRU]
- Site's primary support needs
- Local cost estimates
- Regional specific considerations

Survey responses were received from 27 sites

- 13 EFACTS, 12 FACOMS and 2 new sites
- All sites / investigators have research experience in both observational studies and interventional trials
- 25 with experience in drug trials
- 17 with wearable/device trials
- 13 sites with >50 FA patients at their location

Work group meetings have been consistently attended by over 35 participants representing 12 countries. Individual summaries of workgroup progress to date can be found on page 3.

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The full group was able to meet in person and virtually on November 1st at International Congress for Ataxia Research (ICAR) in Dallas and was lucky enough to have some advocacy representatives join to observe the meeting as an official introduction to this initiative.

The steering committee and work groups have been meeting since early in 2022 to align on priorities for the FA GCC.

Figure 3: FA GCC Investigators Virtual and In Person Nov 01, 2022 at ICAR

Work Group Meetings

Scientific Steering Committee: The FA GCC steering committee has been crucial in making the connections needed to leverage existing staff and relationships, informing decisions on establishing working committees, laying out the structure, governance, and scientific priorities to ensure balanced global perspectives, including those at the patient level. Going forward they will continue meet regularly to define a collaborative research agenda, strive to facilitate new study and analysis ideas, and ensure the continuing scientific integrity and rigor of Consortium facilitated projects.

Pediatric & Pre-symptomatic: Pediatric work group has prioritized the importance of including controls for comparison to pre-symptomatic participants through the natural history study. Their work continues with the goal to identify early biomarkers and clinical outcome measures that can be used in the pediatric population.

Cardiac: The cardiac work group has been discussing methods to obtain the highest quality data collected uniformly across sites.

Late Stage: The late stage group has focused on reducing the burden of research assessments on participants while maximizing existing contributions and data. The group made recommendations for use of the ancillary speech, vision, and upper arm dexterity assessments for participants in this subgroup.

Cognition & Mood: This workgroup has initiated an in-depth discussion of available scales that will be most informative for use in FA, looking at historic use, current trial scales and those used in other disease states.

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Harmonization: The harmonization work group has aligned on the core assessments that will be most valuable to include in the harmonized natural history study. They have defined criteria and a flexible structure that allows for collection of additional ancillary assessments, a design that will facilitate incorporating new measures as they become relevant, such as new PROs or wearable devices collecting patient data at home.

The harmonization group has aligned on a finalized protocol for the UNIFAI Study.

	Core	Non-core/Ancillary	Sub-study	New/Experimental
Definition	Completed, or at least attempted for all patients at every visit	Optional data collection specific to a subgroup of patients or sites, to be used selectively and consistently	Focused, separate, and in-depth protocol at a subset of sites	Assessments not currently collected in the Natural History Study
Goal	Optimizing energy and resources by focusing on the scientific outcomes that capture relevant natural history and inform clinical trials.	Increased ability to analyze factors that influence the course of disease in specific substrata of patients. Maintains flexibility to accommodate regulations, healthcare systems across countries.	Flexibility for investigators to pursue innovative ideas – and efficiently capture data from such experiments so new hypotheses benefit fully from prior work.	Adapt to, and succeed amidst, changing trends in the landscape – e.g., gene therapies, digital health technology, evaluation of pre-symptomatic patients.
Criteria	Items from existing natural history study, established evidence, outcomes useful in clinical trials that can be completed by all sites	Valuable items from existing natural history study specific to a subgroup of patients or limited to certain sites due to pricing, equipment, regulation, or translation.	Work groups able to do more exploratory pilot studies. Encouraged to test out new assessments at the few site level.	Assessments not already collected in the Natural history protocols will be tested out under sub-studies or ancillary subgroups until enough data is available to justify collecting in the full protocol cohort.

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UNIFAI - Harmonized Global Natural History Study

The work groups have developed a harmonized global study protocol, The UNIFAI Study, that specifies a core set of assessments to be collected globally as well as a flexible set of ancillary assessments. The ancillary/optional data collection may be specific to a subgroup of patients or site's capabilities. Ancillary assessments are intended to be used selectively and in a manner that will allow for useful analysis (consistently). A summary of the assessments that have been defined as core and ancillary under this protocol can be found below.

Core Data Collection

- Demographics and Socioeconomic Details
- Medical, Surgical, Medication, Clinical Trial Participation History
- Family FA History
- Vitals Signs
- FA review of signs and symptoms
- FA Diagnosis Details
- Genetic confirmation including repeat size or mutation
- Bio sample collection
- mFARS and/or SARA
- 9-hole peg test
- Timed 25 foot walk / 8 meter timed walk
- Functional Staging for Ataxia
- Patient Reported Outcomes

Ancillary Data Collection

- INAS
- Berg Balance Test
- Timed Up and Go
- Timed 1-minute Walk
- Low Contrast Letter Acuity
- Redenlab speech assessment
- Verbal fluency
- Ocular Coherence Tomography
- Ataxia Instrumented Measures (Cup, Spoon, Pendant)
- Composite Cerebellar Functional Severity (CCFS)
- Symptom Specific Patient Reported Outcomes

Special Event forms

To always be collected when available

- Cardiac Event (Intervention, ECG, Echo, Holter Monitoring), Scoliosis Surgery, Pregnancy, Hospitalization >24 hours, or Mortality

The harmonization group has also been working on global standardization of clinical assessments in FA. The work group has aligned on an updated guidance document for administering the FARs & mFARs, and this 2023 version of the test guidelines will be distributed to member sites in the coming months.

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Data Platform:

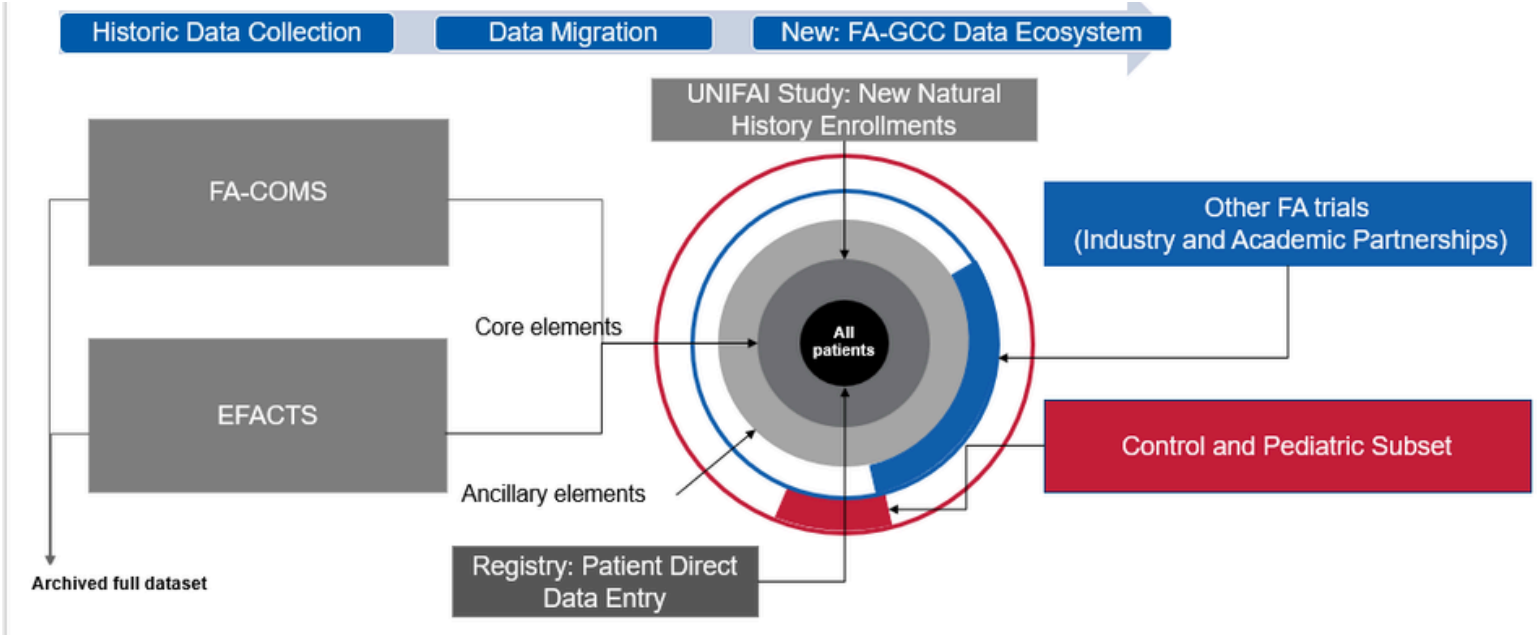

Figure 4: FA GCC Data Platform can support multiple study types

One of the long-term goals identified by the FA GCC was the ability to adapt to, and succeed amidst, changing trends in the landscape such as intervention studies, wearable digital health technology, and virtual visit capabilities.

In order to build a sustainable data ecosystem that supports the FA community in the long-term, a request for proposal outlining the requirements and capabilities the FA GCC was searching for in a database vendor was circulated in September.

Global compatibility, regulatory compliant process, usability of consortium collected data and reduction of redundancy were important in the decision-making process when looking for a new data capture solution. A new database partner, Medrio, has been identified to support FA GCC studies. The new data platform will house the historical data from both natural history studies and facilitate prospective collection under the UNIFAI study.

medrio

Key Medrio Capabilities

- Electronic Consent
- Electronic Patient-Reported Outcomes (ePRO)
- Virtual Visits
- Patient Portal (Engagement)
- Multilingual User Interface
- GDPR compliant, servers in EU and US
- Visual and Intuitive Reporting
- Easily Customizable

HIPAA COMPLIANT · GAMP · EU GDPR COMPLIANT · ISO 27001 · FDA 21 CFR Part 11

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What's to come

Invitation packets for participation in the UNIFAI Study (final protocol, consent template, budget and contract documents) will be distributed to member sites as soon as they are ready, expected March 2023.

Transition to UNIFAI: Formal transition instructions will be provided to the sites active in the EFACTS or FACOMS studies. These will include detailed guidance on the process of transitioning from the current natural history study to the UNIFAI study. Until local ethics approval is granted for the UNIFAI version of the natural hisotry study protocol, all visits should be planned and scheduled as usual under your current study protocol version.

For participants enrolled in EFACTS or FACOMS all visits should be planned and scheduled as usual under your current study protocol.

Prepare updated documents
- submissions to IRB or EC
- contract updates

Sites will discontinue their current protocol version and begin scheduling visits under the new UNIFAI protocol only once all steps below have been completed.
- IRB/ EC approval
- Protocol Training
- Trial Agreement Executed

Participate

Call to global patient advocacy organizations interested in joining the **FA GCC Patient Advocacy Advisory Board**. Please nominate a representative and provide their contact information to FAGCC-info@curefa.org

The **Bio sample workgroup** is being established this month, if you or someone from your site would like to participate in this group, provide contact information to FAGCC-info@curefa.org